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American Journal of Obstetrics and Gynecology

VOL. 45 MARCH, 1943 No. 3

American Association of Obstetricians, Gynecologists and Abdominal Surgeons

Fifty-Fifth Annual Meeting, September 10 to 12, 1942

PRESIDENTIAL ADDRESS

FACTORS INFLUENCING THE GEOGRAPHIC DISTRIBUTION OF THE OBSTETRICIAN-GYNECOLOGIST*

GRANDISON D. ROYSTON, M.D., ST. LOUIS, MO.

ON THIS, the Fifty-Fifth Annual Meeting of our Association, we find the very existence of the nation and every one of our people gravely threatened. Regardless of the outcome of this struggle, it is evident that our lives will be changed radically in the future. As members of a thoughtful profession, we can, we must, we will adjust ourselves to the needs of our country and of our people.

Dr. Palmer Findley, a former president, suggested to me last year that the geographic distribution of the obstetrician-gynecologist might be of interest as the subject of my address to you at this time. Although this subject seemed at first rather remotely connected with medical education, it has proved otherwise. The growing tendency of the government to provide medical care, to which our profession has seemed somewhat indifferent, indicates the importance of a more serious consideration of the problem.

The Directory of Medical Specialists, in its last edition, published in 1940, shows that although 11.3 per cent of the total population of the United States resides in cities with a population under 5,000 as compared with 12.3 per cent residing in cities of over 1,000,000, the latter have nine to ten times the number of certified specialists.

*Presidential address at the Fifty-Fifth Annual Meeting of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, Hot Springs, Va., September 10 to 12, 1942.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Lee-Jones (*Fundamentals of Good Health*[1]) estimates that one physician, devoting 2,000 physician hours per year, could care for all the obstetrics in a community with a population of 7,332, with 23.56 pregnancies per 1,000 general population. These writers state that this does not allow for anything other than the time actually spent with the patient. They further estimate that 100 pregnancies will result in 86 deliveries (83 live births and 3 stillbirths), while 14 will abort. Of the 86 terminating in birth, they feel that the general practitioner can deliver all but nine, who require an obstetrician.

TABLE I. FROM LEE-JONES' FUNDAMENTALS OF GOOD HEALTH (IN 1932)

		PER CENT OF ALL CASES REQUIRING MEDICAL CARE	PER CENT OF ALL PHYSICIANS' HOURS
Puerperal state		2.52	14.05
Female genitourinary		1.71	2.56
Total		4.23	16.61
	PHYSICIAN HOURS PER 100,000 POPULATION. TIME ACTUALLY SPENT WITH PATIENT	PHYSICIANS REQUIRED	
		PER 100,000 POPULATION	FOR UNITED STATES
Prenatal care	8,611	4.31%	5,293
Delivery and postpartum care	18,660	9.33%	11,457
Total	27,271	13.64%	16,750

Table I from Lee-Jones shows that 4.23 per cent of all patients are obstetric-gynecologic and consume 16.61 per cent of the practitioner's time. However, their estimate of the time actually spent with the patient might be compared with the time needed for the management of an industry to sign a contract to supply a customer. The actual signing of the contract is insignificant as compared with the time and study needed in the preparation of the contract and all details appertaining thereto. They estimate that the time required for prenatal care will require of the physician 3.66 hours per patient, while delivery and postpartum care by the physician will require 7.92 hours per patient. While these figures represent only the estimated time actually spent with the patient, who will render the decision when such split-second timing will require that such service be rendered? It would seem that such deliveries would have to be made on a time schedule, and where and how is the practitioner trained to make such decisions?

The Associated Press in July, 1942, quoted figures from the Federal Procurement and Assignment Service showing that 89,862, or 51 per cent, of the 176,200 physicians in the nation are listed as specialists. In 1930, there were 40,000 specialists, or about 30.5 per cent, among 112,000 physicians.

In the care of patients, it is taken for granted that every graduate is capable of doing general practice at the time of graduation; that he is competent to practice general medicine, pediatrics, surgical diagnosis,

minor surgery, and first aid in emergencies, and normal obstetrics, subjects stressed for the intern year. This is wishful thinking when our medical schools now graduate men not yet safe practitioners of the branches mentioned, and who aspire to become specialists before they have had this basic training. If the practitioner will avoid all meddlesome interference in obstetric cases and, if in any doubt as to what course to pursue, will do nothing, the end results will be generally good. The great majority of all difficulties encountered in obstetrics result from unwise interference. For this reason, it is the responsibility of medical schools to graduate only those fully competent to diagnose, discriminate, and treat properly such a large proportion of normal obstetric patients.

The gynecologic care of patients by the recent graduate of today is naturally influenced by his training in medical school. Most of this training is in the care of gross pathologic conditions and operative cases, hence the tendency to consider every patient an operative case. Too little time and thought are given to functional disturbances which the Committee on Medical Education states may be due to or aggravated by social and economic conditions. The judgment and management of gynecologic patients by the general surgeon or the general practitioner often lead to abortive and misdirected procedures for which no skill in technique will compensate. Many schools are wisely using their out-patient departments for such teaching, though too often the great weakness of the modern medical school is in its failure to utilize to the fullest extent the services of experienced clinicians for this purpose. The present-day graduate is more often a laboratory adherent than a close clinical observer. It is believed by many experienced practitioners that an out-patient service approximates closely conditions seen in private practice, yet in obstetrics the present tendency is to reduce the number of home deliveries, where the student and intern can learn to manage normal labor most readily.

The incidence of operated patients applying in an out-patient gynecologic service varies from 3 to 10 or 12 per cent. These figures might be improved, should every hospital require that a written diagnosis and proposed procedure be publicly displayed in the operating room prior to operation. Such a rule would prove highly beneficial in the interest of the patient, the diagnostic study by the operator, and the teaching of interns and students.

The material for this study, an analysis of which I am presenting, is taken from questionnaires mailed to 8,766 physicians in 2,156 different locations. These practitioners either limited their work to, or manifested special interest in, this specialty. The mailing list was obtained from compiling the mailing lists of all national, regional, and available special societies of obstetricians and/or gynecologists, the Diplomates of the American Board of Obstetrics and Gynecology through 1941, the

mailing list of the American Congress of Obstetrics and Gynecology, and the Directory of the American Medical Association.

It is recognized that all of those questioned do not limit their work, yet their various affiliations and connections with the sources from which the lists were compiled, indicate their interest in the specialty. It was felt that a direct expression from physicians actually doing this work throughout every state would be more illuminating than to investigate through educational groups. The latter have too often seemed less closely in touch with the realities faced by the practitioner.

Almost two-thirds (1,405 of 2,156) of all communities questioned had a population of less than 10,000, thus denoting that our specialty occupies an important part in the work of the practitioners residing there. Lee-Jones' estimate is that 16.61 per cent of all physician hours are devoted, as follows: to puerperal state 14.05 per cent; to female genito-urinary diseases 2.56 per cent.

The Committee on Graduate Medical Education of the American Medical Association gives the figures in 1936 for those physicians limiting their work or giving special attention to a specialty as follows: obstetrics 2,437; gynecology 1,169; obstetrics and gynecology 3,792; a total of 7,398. The figures here presented are an attempt to canvass all of this list and also all practitioners having interest in the specialty.

The results of this study are shown in the following tables. Table II shows the number and population of each community questioned as well as the number of practitioners questioned. As might be expected, the larger communities were less numerous, and had the greater number of practitioners questioned.

TABLE II

REPRESENTED IN QUESTIONNAIRE	TOTAL	NO. WITH POPULATION OF:					
		UNDER 10,000	10,000-25,000	25,000-50,000	50,000-100,000	100,000-200,000	OVER 200,000
Communities	2,156	1,405	395	165	95	53	43
Practitioners	8,766	1,631	819	672	719	872	4,053

Table III shows that of the age group under 40, the greatest proportion were reared in communities with a population under 10,000, yet a smaller incidence than in the other two age groups (40-59, and those of 60 years and older). This may have been due to the fact that more of the younger age group were reared in larger communities where many of them remained to practice. Many of this group located in communities where they attended medical school or interned.

Tables IV and V show the trend of more than half to practice in communities other than that in which they were reared. This change is mainly to larger communities. Forty-one and eight-tenths per cent of the men under 40, 54.7 per cent of those from 40 to 59, and 68.6 per cent of those of 60 and over, were reared in communities under 10,000 population. Hence, it is evident that the majority of those in our specialty were reared in smaller communities.

TABLE III. AGE GROUPS UNDER FORTY YEARS

REARED IN COMMUNITY WITH POPULATION OF:		TOTALS		MOVED TO COMMUNITY WITH POPULATION OF (IN PER CENT):					
		NO.	% OF TOTAL	UNDER 10,000	10,000 TO 25,000	25,000 TO 50,000	50,000 TO 100,000	100,000 TO 200,000	OVER 200,000
Under 10,000		186	41.8	0	15.6	14.0	21.5	9.7	39.2
10-25,000		79	17.7	13.9	0	12.8	15.0	11.4	46.8
25-50,000		56	12.6	14.3	8.9	0	25.0	14.3	37.5
50-100,000		31	7.0	9.7	16.1	16.1	0	12.9	45.2
100-200,000		28	6.3	14.3	10.7	7.1	7.1	0	60.7
Over 200,000		65	14.6	20.0	24.6	21.5	21.5	12.3	0
Totals	No.	445							
	%		100.0	8.8	13.0	12.8	18.4	10.6	36.4

TABLE IV

REARED IN COMMUNITY WITH POPULATION OF:		TOTALS		MOVED TO COMMUNITY WITH POPULATION OF (IN PER CENT):					
		NO.	% OF TOTAL	UNDER 10,000	10,000 TO 25,000	25,000 TO 50,000	50,000 TO 100,000	100,000 TO 200,000	OVER 200,000
Under 10,000		481	54.7	0	13.1	12.4	13.5	14.3	46.6
10-25,000		146	16.6	6.2	0	17.1	9.6	13.0	54.1
25-50,000		71	8.0	5.6	11.3	0	16.9	16.9	49.3
50-100,000		58	6.6	5.2	6.9	13.8	0	22.4	51.7
100-200,000		54	6.1	11.0	1.8	16.7	7.4	0	63.0
Over 200,000		70	8.0	15.7	20.0	20.0	18.6	25.7	0
Totals	No.	880							
	%		100.0	3.7	10.2	13.2	12.3	14.9	45.7

TABLE V. AGE GROUPS OVER SIXTY YEARS

REARED IN COMMUNITY WITH POPULATION OF:		TOTALS		MOVED TO COMMUNITY WITH POPULATION OF (IN PER CENT):					
		NO.	% OF TOTAL	UNDER 10,000	10,000 TO 25,000	25,000 TO 50,000	50,000 TO 100,000	100,000 TO 200,000	OVER 200,000
Under 10,000		168	68.6	0	18.4	12.5	11.9	8.9	48.2
10-25,000		27	11.0	18.5	0	11.1	11.1	18.5	40.7
25-50,000		22	9.0	13.6	13.6	0	4.6	4.6	63.6
50-100,000		5	2.0	20.0	0	0	0	40.0	40.0
100-200,000		9	3.7	0	0	0	11.1	0	88.9
Over 200,000		14	5.7	28.6	21.4	14.3	28.6	7.1	0
Totals	No.	245							
	%		100.0	5.3	15.1	10.6	11.8	9.8	47.4

Table VI shows the replies accordingly to the age groups of those who remained in localities similar to those in which they were reared as well as the number who changed.

Table VII shows the present distribution of practitioners replying to the questionnaire. This suggests that there are opportunities and needs for trained obstetricians and gynecologists in communities with populations ranging from 25,000 to 200,000.

Table VIII shows the factors that influenced the choice of present location. Desirable hospital facilities ranked first among the total replies, followed by desirable professional connections, home town, etc.

TABLE VI

AGE GROUPS	TOTALS		NO. LIVING IN LOCALITIES WITH POPULATION SIMILAR TO PLACE REARED		NO. MOVING TO LOCALITIES WITH POPULATION DIFFERENT THAN PLACE REARED	
	NO.	%	NO.	%	NO.	%
Under 40 yr.	939	31.6	493	52.5	446	47.5
40-59 yr.	1,610	54.3	730	45.3	880	54.7
60 yr. and over	417	14.1	172	41.2	245	58.8
Totals	2,966	100.0	1,395	47.0	1,571	53.0

TABLE VII

POPULATION GROUPINGS		NO CHANGE IN LOCATION OR POPULATION STATUS (IN PER CENT)			MOVED TO COMMUNITY WITH CHANGE IN POPULATION STATUS (IN PER CENT)		
		UNDER 40 YR.	40 TO 59 YR.	OVER 60 YR.	UNDER 40 YR.	40 TO 59 YR.	OVER 60 YR.
Under 10,000		9.5	18.8	37.8	8.5	3.7	5.3
10-25,000		7.1	6.0	5.8	13.7	10.2	15.1
25-50,000		6.3	5.2	5.2	12.3	13.2	10.6
50-100,000		7.3	6.9	3.5	18.4	12.3	11.8
100-200,000		9.3	10.1	5.8	10.8	16.0	9.8
Over 200,000		60.5	53.0	41.9	36.3	45.6	47.4
Total	% of total	35.3	52.4	12.3	28.4	56.0	15.6
	No.	493	730	172	446	880	245
	No. in group	1,395			1,571		

TABLE VIII

CHOICE OF PRESENT LOCATION WAS INFLUENCED BY:	TOTALS		AGE GROUPS (IN PER CENT)		
	NO.	% OF TOTAL (2,966)	UNDER 40 YR.	40 TO 59 YR.	OVER 60 YR.
Desirable hospitals	1,492	50.3	27.8	57.8	14.4
Desirable professional connections	1,281	43.2	29.5	56.3	14.2
Home town	1,077	36.8	32.0	56.6	11.4
Desirable environment to rear family	934	31.2	26.1	55.0	18.9
Location near relatives	710	24.0	32.7	53.2	14.1
Desirable teaching connection	700	23.6	31.8	54.6	13.6
Opportunity to make money	641	21.6	25.6	53.5	20.9
Environment suitable to health	373	12.6	21.2	52.3	26.5
Desirable group practice	229	7.7	33.1	52.0	14.9
Other reasons	214	7.2	27.6	53.8	19.6

Among the younger group, desirable group practice, location of near relatives, and home town influenced the choice of present location, in the order named. Among the older group (60 and over), an environment suitable to health, the opportunity to make money, and a desirable environment in which to rear a family were the most common factors influencing the choice of present location.

Among all age groups, the opportunity to make money ranked sixth. Other reasons were a desirable place in which to live, climate, cultural attractions, recreational opportunities, etc., while three wrote "to get away from wife's relatives."

Tables IX, X, XI, and XII show the factors indicated in the order of choice for making smaller communities more desirable locations. All

TABLE IX. AGE GROUPS UNDER FORTY YEARS

FACTORS	TOTALS		ORDER OF CHOICE (IN PER CENT)								
	NO.	% OF TOTAL	1	2	3	4	5	6	7	8	9
Adequate hospital facilities	719	16.9	60.1	18.4	11.0	6.5	2.2	1.1	0.7	0	0
Environment economically able to support specialist	641	15.0	46.5	23.7	15.1	6.4	3.3	3.1	1.3	0.6	0
Public trained to cooperate with specialist	638	14.9	38.7	20.5	18.0	10.8	4.9	3.9	2.1	1.1	0
Congenial professional associations	538	12.6	26.6	9.9	12.6	13.9	15.6	13.4	5.6	2.4	0
Accessibility to medical centers	459	10.7	23.3	5.5	11.3	13.9	12.4	11.6	17.7	4.1	0.2
Economic stability	451	10.6	19.8	10.6	17.5	16.9	15.5	11.5	6.4	1.6	0.2
Ample transportation facilities	450	10.5	20.1	13.5	15.0	14.9	11.8	9.3	10.7	4.7	0
Proximity to good schools	330	7.7	16.1	1.8	5.8	6.1	8.5	12.4	15.1	33.6	0.6
Other desirable factors	46	1.1	39.1	4.4	6.5	6.5	2.2	2.2	4.3	10.9	23.9
Total No. of choices in 939 replies	4,272	100.0									

TABLE X. AGE GROUPS FORTY TO FIFTY-NINE YEARS

FACTORS	TOTALS		ORDER OF CHOICE (IN PER CENT)								
	NO.	% OF TOTAL	1	2	3	4	5	6	7	8	9
Adequate hospital facilities	1,348	16.9	76.1	12.0	6.8	2.7	1.5	0.3	0.3	0.1	0
Environment economically able to support specialist	1,166	14.7	46.4	24.6	14.0	7.4	3.2	1.9	1.7	0.8	0
Public trained to cooperate with specialist	1,037	13.0	35.8	15.7	20.1	10.7	7.3	5.6	2.8	2.0	0
Congenial professional associations	970	12.2	30.6	6.9	12.1	17.6	11.8	10.8	7.2	3.0	0
Accessibility to medical centers	918	11.6	30.3	4.6	10.8	10.6	12.4	11.5	13.6	6.2	0
Ample transportation facilities	881	11.1	30.2	21.2	13.1	12.2	9.3	7.0	4.2	2.8	0
Economic stability	813	10.2	25.3	8.1	14.9	17.2	14.1	10.6	6.5	3.3	0
Proximity to good schools	691	8.7	27.8	2.2	5.2	6.9	9.8	10.1	15.1	22.9	0
Other desirable factors	130	1.6	54.6	3.8	3.8	7.7	3.1	2.3	1.6	2.3	20.8
Total No. of choices in 1,610 replies	7,954	100.0									

age groups agree that first, adequate hospital facilities must be available; and second, the environment must be economically able to support a specialist, while a public trained to cooperate with a specialist, congenial associations and accessibility to medical centers, closely followed. The older age group place ample transportation facilities fourth among their choices. It is emphasized in many of the private comments that congenial professional associations are desired not alone for personal and professional contacts in obstetrics and gynecology, but also for avail-

able consultation in other branches. Where the choice of factors was indicated by a check of several factors and was not enumerated, all factors checked were given equal importance in the tabulations. A desirable place in which to live or to rear a family, and desirable climate were also considered important factors, as well as desirable religious environment, and by no means least was the expressed desire to locate where there are many physicians who will refer patients.

TABLE XI. AGE GROUPS OVER SIXTY YEARS

FACTORS	TOTALS		ORDER OF CHOICE (IN PER CENT)								
	NO.	% OF TOTAL	1	2	3	4	5	6	7	8	9
Adequate hospital facilities	345	16.9	83.5	10.1	2.0	2.6	0.3	0.9	0.6	0	0
Environment economically able to support specialist	272	13.3	62.5	15.1	11.7	5.9	2.2	1.1	1.5	0	0
Congenial professional associations	261	12.8	51.0	6.1	10.3	8.4	7.3	11.5	2.7	2.7	0
Ample transportation facilities	250	12.2	57.2	18.0	7.2	5.2	5.2	2.4	3.6	1.2	0
Accessibility to medical centers	234	11.5	52.6	4.7	7.2	9.0	6.0	9.0	8.5	3.0	0
Proximity to good schools	215	10.5	53.9	1.4	6.5	5.1	8.0	6.0	6.5	12.6	0
Public trained to cooperate with specialist	215	10.5	49.8	7.4	16.8	14.4	3.7	2.3	3.3	2.3	0
Economic stability	211	10.3	49.3	7.6	7.6	10.0	16.1	4.7	3.8	0.9	0
Other desirable factors	40	2.0	67.5	10.0	5.0	2.5	2.5	5.0	2.5	5.0	0
Total No. of choices in 417 replies	2,043	100.0									

TABLE XII. FACTORS INDICATED IN ORDER OF CHOICE FOR MAKING SMALLER COMMUNITIES MORE DESIRABLE LOCATIONS (TOTALS, ALL AGES)

FACTORS	TOTALS		ORDER OF CHOICE (IN PER CENT)								
	NO.	% OF TOTAL	1	2	3	4	5	6	7	8	9
Adequate hospital facilities	2,412	16.9	72.6	13.6	7.4	3.8	1.5	0.6	0.4	0.1	0
Environment economically able to support specialist	2,079	14.5	48.5	23.1	14.0	6.9	3.1	2.2	1.5	0.7	0
Public trained to cooperate with specialist	1,890	13.2	38.4	16.4	19.0	11.1	6.1	4.7	2.6	1.7	0
Congenial professional associations	1,769	12.4	32.4	7.7	11.9	15.1	12.3	11.7	6.1	2.8	0
Accessibility to medical centers	1,611	11.3	31.5	4.8	10.4	11.3	11.5	11.3	14.0	5.1	0.1
Ample transportation facilities	1,581	11.0	31.6	18.5	12.7	11.8	9.4	7.0	5.9	3.1	0
Economic stability	1,475	10.3	27.1	8.7	14.6	16.1	14.9	10.0	6.1	2.4	0.1
Proximity to good schools	1,236	8.9	29.2	1.9	5.6	6.4	9.1	10.0	13.6	24.0	0.2
Other desirable factors	216	1.5	53.7	5.1	4.6	6.5	2.8	2.8	2.3	4.6	17.6

Specially trained obstetricians and gynecologists seem to obtain their patients largely from one of three sources: (1) referred by other phy-

sicians; (2) through institutional connections; (3) referred by well-satisfied former patients. Although customs vary in different communities, in most instances the last source is easily the most dependable and least likely to undergo changes. References from other physicians are likely to be from one's contemporaries, and when the ripeness of age and experience should be most desirable for the patient's welfare, often many of the contemporaries have died, ceased to practice, etc. Institutional sources of supply may sometimes require too much political effort to maintain oneself.

This inquiry has attempted to reach every practitioner in the United States listed as being interested or specializing in obstetrics and/or gynecology. The response of more than 33 per cent is encouraging as compared with the customary 25 per cent of responses reckoned by statistical institutions. In addition to the replies tabulated, a number could not be used for reasons of being too incomplete, death of party addressed, illegibility, and one reply from West Virginia stating, "This is the silliest of all silly questionnaires I have ever seen; it is not worth an answer." All other responses were helpful and cooperative.

Eight hundred and sixty-six, or more than 29 per cent of the replies brought additional voluntary information varying from a few words to letters of several pages. These voluntary comments suggest that the background, education, and preparation of the physician often may exert a marked influence on his choice of location. Many replies state, "I attended medical school and located here; these are the reasons for my present location." Another stated "after being regimented through medical school and hospital for nine or ten years, I felt the need of being told what to do, so remained where I could be directed." Another, aged 31, wrote, "I am afraid to get away from the place where everything has been planned for me." Such statements raise the question as to whether the present medical school is developing in its graduates the proper initiative. The general belief is that the function of the medical school is to train doctors to treat sick people.

The Commission on Graduate Medical Education, consisting of twenty representative educators, was organized in 1937 and published its report in 1940. This report recognized that the stress and strain of modern society cause functional disturbances, often of social and economic origin, or aggravate them, that may mask or simulate organic disease. How much this is being taught to students today is debatable. This report advocates that the intern year should be used for training in general medicine, normal obstetrics, pediatrics, surgical diagnosis and first aid in emergencies, while surgical technique should be reserved for the residency.

The modern medical school seems to have demanded of a departmental head: (1) the production of investigative work; (2) that he be an able teacher; (3) a capable clinician; (4) an executive; (5) have ability to satisfy the trustees, public, etc., and often raise money for his institu-

tion. Such perfection in one individual rarely exists. The result has often been disillusionment and disappointments to all parties concerned. The rare individual with a truly creative mind and love for research should receive every facility for pursuing his investigations. In my opinion, he should receive the highest salary among his colleagues of similar rank in his institution. Too often his talent as an investigator is not well utilized, while his time is dissipated by too many hopeless demands of minor consequence.

It is indeed a poor criticism that offers no suggestion for improvement. It is probable that medical schools of the future will receive less endowment and in some instances may be forced to obtain governmental aid to exist. If such aid is to be forthcoming, medical schools must realize and really discharge their functions better if they are to justify the reasons for their existence. The present outlook for adequate financial support from private sources is doubtful, and the necessity of governmental aid may have to be considered. This aid is likely to depend upon the ability of the medical schools to graduate an adequate supply of capable physicians for ample medical care to every community. The following suggestions are offered with this hope:

1. The office of dean should receive sufficient salary to attract a capable executive and administrator, who will devote full time to the office. He should be thoroughly familiar with all that transpires in every department. He must insist that every departmental head organize his department properly and work harmoniously with all other departments to the benefit of his institution and its products (students, alumni, research, etc.). He should interpret the medical school to the public.

2. Departmental heads should be selected on the basis of their ability to excel in the branch they expect to teach. The basic science branches should be headed by men expert in such branches, while clinical departmental heads should be primarily expert clinicians and executives with full appreciation for research. They should see that every member of their departments makes some annual contribution. With few exceptions, our specialty has been taught best by those who were primarily good clinicians. Perhaps less than 2 per cent of the student body is interested in, or capable of, developing into research investigators, and medical schools should be more cognizant of this fact in the interest of the more than 98 per cent of students who are being trained to treat sick people.

3. In view of the vast field of medicine and the general recognition of the inability of any medical school to graduate in four years a man safe to practice medicine, thirteen states in this country and four Canadian schools (up to 1939) require a fifth year of internship before graduation. On all sides may be found criticisms of the late age at which men in full possession of their faculties become fully active

members of their communities. Professor H. C. Sherman has pointed out that by the time a professional man has finished his schooling, about one-third of his life has passed; another third will be spent in proving to himself and to others what he is able to do, and in most cases not until he is approximately fifty years old does he attain to a post of high responsibility and is given the fullest opportunities to do his work.

Professor H. C. Lehman has found that the majority of outstanding contributions by physicists, chemists, and inventors were made at 30 to 34 years of age. His investigation convinced him that the prime of life occurred in adolescent or early adult life, and he concluded that the greatest mental productivity was on the average recorded at the age of thirty.

The present-day graduate from medical school is not now able to begin private practice until this late age. The undesirability of such prolonged preparation has been sounded by President Lowell of Harvard University and President Butler of Columbia University, while President Hutchins of Chicago University feels that in many instances the collegiate education should terminate at the end of two years. Dr. J. P. Simonds of Northwestern University in the June, 1940, issue of the *Marquette Medical Review* sounded a highly pertinent note when he stated that the general practitioner, of all of our citizens, can do more to save medicine from socialization than any other group. This threat looms much more ominously over us today than in 1940, yet it is doubtful if our medical schools are fully alive to this danger of political control.

The value of a college education prior to admission to medical school requires no argument. The results speak for themselves in all walks and professions. With no desire to lower standards, yet with an earnest hope to improve the training of medical graduates who should spend more of their time being trained in the work that they expect to do, I would like to see every student admitted to medical school only on the following basis:

1. Individual selection, preferably after a personal interview by a personnel committee on admissions. Such committees could be appointed by each medical school, and interview each applicant at stated times and places similar to specialty board examinations. The applicants might be graded A, B, C, and the results pooled through a common clearing house of all the schools. If possible, the college and the high school should collaborate with the medical school in the applicant's preparation through the last two years of high school and the first two years of collegiate work. Some mistakes in admissions will always occur, yet individual selection after a personal interview together with the applicant's past record, should limit these errors.

2. Applicants would be eligible for admission to medical school after two or more years of college work. The crowding of four years' collegiate

work into two and one-half or three calendar years is best suited for emergencies, since vacations are needed to prepare the student for the work ahead under normal conditions.

3. Scholarships or loan funds should be made available for every needy student who shows unusual ability or interest in investigative work. It must not be forgotten that clinical research, as emphasized by Heaney in commenting on Sampson's work on endometriosis, is fully as important as chemical research.

4. Every student, following four years' work in medical school, shall serve two additional years of rotating internship including out-patient work in a hospital under the supervision of his medical school before graduation. This would necessitate closer affiliation between the medical schools and the hospitals of their communities to their mutual advantage. This experience is as desirable for the medical school as it is for student or intern. It would make possible the graduation of better trained physicians *really competent* to be safe general practitioners at an age not necessarily greater than that at which they now graduate without an internship. Residencies and assistant residencies can be used to perfect the training of the specialist. Such specialists would be better trained because of this compulsory two-year rotating internship and externship that too few of them now have.

If the medical profession desires to provide adequate medical care for *all* the people of this country, the suggestions just made offer a way to make a safe and competent general practitioner of every graduate when he receives his diploma.

The results of the analysis of this questionnaire indicate that we cannot hope to have an equitable geographical distribution of certified specialists in every community. However, we can insure that every practitioner has received adequate training for safe obstetric and gynecologic care before graduation. Such universal training should qualify every graduate, wherever he locates, as an asset in our field.

Let us hope that a sane and practical solution of our problem will keep our profession out of the realm of the politician and of political control. A better geographic distribution of better trained practitioners is essential to this end.

I am indebted to my secretary, Miss Helen Schroeder, for compiling and arranging this mailing list as well as other helpful and laborious work. Classifying and tabulating the return replies was done with the help of my helpmate, Eunice W. Royston.

Reference

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THE EFFECT OF PREOPERATIVE IRRADIATION ON ADENOCARCINOMA OF THE UTERUS*

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IN 1935 a Y-shaped radium filter was described[15] which we feel was an improvement over the methods in vogue at this time.[1-3, 5, 9, 13] The equal intensity curves and the calculation of the radium dose in roentgens were given. Since this method was adopted in our clinic, 77 patients with adenocarcinoma of the uterine fundus have been admitted to our service. It was, therefore, considered of interest to study these cases to determine the effect of this type of irradiation on the carcinoma and to compare those patients who were irradiated by what we considered an adequate dose with those inadequately treated according to our standard.

Material Studied

Of the 77 patients 11 were hysterectomized after various time intervals following irradiation treatment and the effect of the irradiation on the tumor and the uterus was studied. Five of these patients were considered adequately treated according to our described technique and in none of these uteri was carcinoma found. The remaining 6 cases, inadequately irradiated, in our opinion, all showed carcinoma. Twenty patients were irradiated but not hysterectomized. Ten of these had one or more curettages to determine the presence or absence of active disease. Again it was the finding that those cases treated according to our technique were most likely to be free of detectable carcinoma. A third group of 7 cases had been diagnosed as adenocarcinomas by other pathologists but we were unable to obtain tissue for grading or verifying the diagnosis. In each instance, however, the referring physician was considered dependable. Five in this group had curettage following irradiation and one had a panhysterectomy. The remaining 39 cases were excluded from this study because they were hysterectomized and then irradiated.

Technique of Adequate Irradiation

All patients are curetted and the Y capsule containing 50 mg. of radium element in each arm is immediately inserted into the uterine cavity. The width of the uterine fundus has been determined and the capsule opened as described in the original article. After 2,000 mg. hours the capsule is removed. On the eighth and sixteenth days this radium dose is repeated. This gives a total radium dose of 6,000 mg. hours. The isadose curves and r. dose have been published and will not be repeated

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here. On the days that the radium is not in the uterus the patient receives x-ray therapy.

The factors used in the production of the roentgen ray are 800 kilovolt maximum obtained from a double pulsating villard current, a load of 10 milliamperes on the x-ray tube, which is rendered gas free by oil vacuum pumps, a water-cooled tungsten target, a filter equivalent of 10 milliamperes of copper, a focal skin distance of 70 or 86 cm., field sizes varying from 10 to 20 square cm., and a half value layer of 8.2 mm. of copper, corresponding to an average wave length of 0.028 or a minimum wave length of 0.0128 angstrom unit. The output of roentgens per minute measured with a thimble chamber is 36 roentgens without and 44 roentgens with backscatter. The dose attained at a depth of 10 cm. measured in a bakelite phantom is 56 per cent of the surface intensity if the size of the entrance field is from 300 to 400 square cm. Whenever practicable the number of fields is two, namely pubic and sacral. If the patients had an anteroposterior diameter of 23 cm. or more, three or four fields were used. The amount of radiation required to produce a tolerance skin dose with 800 kilovolt roentgen rays is 4,000 roentgens if applied in ten fractions at forty-eight-hour intervals. If two fields are used, the midpelvic dose is the same as that attained on the skin, or about 4,000 roentgens, at the lateral bony pelvic walls as well as in the midpelvis. The rate of recovery of the tissues after each fractional dose has not been subtracted. The rate of recovery of the normal tissues in contradistinction to the abnormal ones is as yet not known. The dose attained within the pelvis after twenty-eight days was 4,000 roentgens, with backscatter.

Clinical Grouping

The clinical grouping of Schmitz[16] was used to classify these cases as to the extent of the disease.

Clinical Group I.—The cancer is clearly localized. The growth not larger than 1 cm. in diameter may be said to be clearly localized. The uterus is freely movable. The form and consistency are normal.

Clinical Group II.—The tumor is about 2 to 3 cm. in diameter. The uterus is freely movable. Palpation elicits an area of infiltration or nodulation in the walls accompanied by a corresponding increase in size of the body.

Clinical Group III.—The tumor invades about one-half of the body. The size is perceptibly increased and irregular. The consistency is firmer than normal, especially within the planes of the growth. Subserous nodes are felt plainly. The mobility of the uterus is decreased, the inguinal or hypogastric lymph nodes may be enlarged but are movable.

Clinical Group IV.—Comprises the totally carcinomatous uterus with invasion of the adjacent structures, especially the parametria and lymph nodes. There is fixation of the tumor mass and the metastases. Fixation is always characteristic of advanced and terminal cancers.

Method of Studying the Removed Uteri

At the time this report was in preparation there were available for detailed study four of the five uteri, in which after radiation no tumor could be found microscopically in routine sections. These four uteri

were sectioned longitudinally at right angles to the mucosal lining so that practically the entire lining of the cervix and of the body of the uterus was included in blocks varying in thickness from 3 to 5 mm. The blocks in all of the four cases included the entire thickness of the wall of the cervix and of the wall of the body near the internal os. In two of the uteri, the entire thickness of the wall of the rest of the body was included in the appropriate blocks; in the other two, only the internal 1.5 to 1.8 mm. of the myometrium were included. The number of blocks obtained from any one of the uteri was not less than 27 nor more than 35. One section was taken from the surface of each block; then each block was cut halfway through and another section taken. Since the original blocks were 3 to 5 mm. thick, the net result was sections of the lining of the uterus and of the adjacent tissues at 1.5 to 2.5 mm. intervals and the total number of microscope slides prepared from any one of these 4 uteri not less than 54 nor more than 70. The tissues were stained with hematoxylin and eosin. For the purposes of this paper, our attention was centered on the exclusion, as far as possible, of any viable tumor in these uteri. An examination of the additional slides prepared from these uteri substantiated the impression gained from the study of the routine sections. No viable tumor was demonstrable. A more detailed report on the gross and microscopic findings in these uteri is being prepared. Only routine sections of uteri which showed carcinoma after irradiation were made. Similar studies have been made by Arneson,[1] Donovan and Warren,[4] and Healey and Brown,[7] but in each instance the dosage of radium was much less than in our series. Phaneuf[12] has shown that the minimum lethal dose for corpus cancer is from five to ten skin erythema units.

Discussion

Table I summarizes the five cases adequately treated in which no carcinoma was found in the removed uteri. Case 2 received but 2,000 mg. hours of radium in the Y applicator. Further radium was not used because of the intense cystitis and proctitis that developed. Whenever the patient develops such a reaction, the dose of radium must be decreased as permanent injury to the bladder or bowel may result. The vagina of these patients is tightly packed while the radium is in place and the bladder kept empty with a retention catheter. An enema should be given routinely before inserting the applicator so as to keep the rectosigmoid empty and as far away from the uterus as possible. In this entire group of cases but one suffered a permanent injury due to the irradiation. This patient (Case 2, Table IV), before entering Mercy Hospital, received in a single dose 6,000 mg. hours of radium in a straight two mm. capsule. Although living, she now has a rectouterine fistula. A capsule of radium left in one position for this single dosage will over-irradiate the tissues in direct contact with the capsule. Patient in Case 5 received but 3,000 mg. hours of radium at Mercy. She had had 1,200 r. of 200 kilovolt x-ray to the skin immediately before admission, and again the reaction was too intense for further radium therapy. The combined dose, however, was considered adequate. In each of the uteri studied, necrosis of the myometrium was demonstrated to variable depths but not over 5 mm. The further radiation changes in the myometrium have been studied and form the basis of another report.

Table II summarizes the six cases inadequately treated in our opinion, and in each instance active carcinoma was still present in the removed uteri. Of interest is the finding of radiation change in the tumor of

TABLE I. SUMMARY OF CASES RECEIVING PREOPERATIVE RADIATION THERAPY

PATIENT AGE GROUP	DIAGNOSIS ON CURETTINGS	RADIUM AND X-RAY	INTERVAL BETWEEN RADIATION AND OPERATION	OPERATION	LABORATORY REPORT	RESULT
A. D. 50 II	Adenocarcinoma Grade II	6,000 mg. hr. Y caps. 4,000 r. x-ray midpelvis	4 months	Vaginal hysterectomy. Bilateral salpingo-oophorectomy	Necrotic polypoid mass 2 × 1 × 1 cm. attached in left cornu; chronic cervicitis. Radiation changes. Healed salpingitis. Atropic ovary. No malignant tumor microscopically	Living and free of detectable disease, 4 yr. 8 mo.
D. C. 38 III	Adenocarcinoma Grade III	2,000 mg. hr. Y caps. 4,000 r. x-ray midpelvis	8 months	Panhysterectomy. Bilateral salpingo-oophorectomy	Ulcer with necrotic margins and base in body just above internal os. Adjacent 5 mm. of myometrium necrotic. Chronic cervicitis. Radiation changes. Left hydrosalpinx. Atrophic ovaries. No malignant tumor microscopically	Living and free of detectable disease, 2 yr. 3 mo.
M. S. 65 II	Adenocarcinoma Grade II	6,000 mg. hr. Y caps. 4,000 r. x-ray midpelvis	4 months	Vaginal hysterectomy. Bilateral salpingo-oophorectomy	Necrotic patch, 6 mm. thick, in lining of body of uterus. Multiple leiomyomas of uterus of moderate size. Adenomyosis of myometrium. Radiation changes. No malignant tumor microscopically	Living and free of detectable disease, 18 mo.
P. G. 52 II	Adenocarcinoma Grade II papillary	6,000 mg. hr. Y caps. 4,000 r. x-ray midpelvis	5 months	Vaginal hysterectomy. Bilateral salpingo-oophorectomy	Necrotic plaque 8 mm. in diameter and 5 mm. thick in lining of uterus at internal os. Necrotic polypoid mass in fundus 1.1 × 0.8 × 0.4 cm. Radiation changes. No malignant tumor microscopically	Living and free of detectable disease, 14 mo.
R. B. 46 III	Adenocarcinoma Grade III	3,000 mg. hr. straight caps. 4,000 r. x-ray midpelvis	3 months	Panhysterectomy. Previous salpingo-oophorectomy	Necrotic plaque in body projecting slightly into uterine cavity and extending just below internal os. Adjacent 3 mm. of myometrium necrotic. Small leiomyoma of uterus. Chronic cervicitis. Radiation changes. No malignant tumor microscopically	Living and free of detectable disease, 2 yr. 9 mo.

TABLE II. SUMMARY OF CASES RECEIVING PREOPERATIVE RADIATION THERAPY

PATIENT AGE GROUP	DIAGNOSIS ON CURETTINGS	RADIUM AND X-RAY	INTERVAL BETWEEN RADIATION AND OPERATION	OPERATION	LABORATORY REPORT	RESULT
E. D. 70 III	Adenocarcinoma Grade III	4,500 mg. hr., straight caps. 4,000 r. x-ray mid-pelvis	3 years	Vaginal hysterectomy Bilateral salpingo-oophorectomy	Adenocarcinoma of endometrium with diffuse invasion of myometrium. Multiple leiomyomas of uterus. Marked radiation changes with absence of much of cervix	Died 3 mo. after operation of metastases
A. L. 42 III	Adenocarcinoma Grade II Areas of squamous metaplasia (adenocanthoma)	2,000 r. x-ray mid-pelvis 1,500 r. x-ray mid-pelvis	2 months	Panhysterectomy Bilateral salpingo-oophorectomy	Large adenocanthomatous ulcer in body extending slightly below internal os. Deep invasion of myometrium. Metastases to anterior lip of cervix and left ovary	No follow-up after 11 mo.
A. V. 70 III	Adenocarcinoma Grade III	4,000 r. x-ray mid-pelvis No radium	8 months	Panhysterectomy Bilateral salpingo-oophorectomy	Polypoid adenocarcinoma 2.5 × 2.5 × 1 cm. in fundus. Invasion of adjacent myometrium. Multiple small leiomyomas. Chronic salpingitis	Living and free of detectable disease, 6 yr.
M. M. 61 II	Adenocarcinoma Grade III	4,000 r. x-ray mid-pelvis No radium Pyometra	3 months	Vaginal hysterectomy Bilateral salpingo-oophorectomy	Adenocarcinomatous ulcer in upper cervical canal. Extension into adjacent coats of cervix and adjacent myometrium. Chronic cervicitis. Radiation changes	Living and free of detectable disease, 14 mo.
T. T. 48 II	Adenocarcinoma Grade III	3,500 mg. hr., straight caps. No x-ray	1 month	Panhysterectomy Bilateral salpingo-oophorectomy	Adenocarcinoma of endometrium with deep invasion of myometrium. Radiation changes	Living and free of detectable disease, 2 mo.
A. M. 42 II	Adenocarcinoma Grade II	1,800 mg. hr., straight caps.	4 weeks	Panhysterectomy Bilateral salpingo-oophorectomy	Necrotic mucosal elevation 4 mm. in diameter in body near internal os. Elsewhere adenocarcinoma confined to endometrium. Radiation changes. Chronic cervicitis. Left tuboovarian abscess	Living and free of detectable disease, 4 yr. 4 mo.

those cases treated with x-ray alone. This demonstrates that external irradiation is of value in the treatment of the primary lesion as well as for its effect on the pelvic cellular tissues and lymphatics. The clinical grouping shows the cases to be almost equally divided into Groups II and III, and the pathologic grading is likewise evenly divided in Grades II and III. Three of the cases found free of disease were in clinical Group II and Grade II carcinomas. One was in Group III and Grade III. The only case to die to date was also in Group III and a Grade III carcinoma. This patient (Case 1, Table II), remained free of symptoms for three years. Then she received a second course of high voltage x-ray therapy and was operated upon. Active disease was found throughout the myometrium, and the patient died three months after operation from metastases to the bowel and liver.

The 11 patients operated upon, after this extensive therapy, presented no increased technical difficulty in performing the surgery. There was no immediate surgical mortality, and only one patient was morbid, this being due to an acute cystitis on the basis of the previous irradiation. At least three months should elapse between the irradiation and the removal of the uterus. This permits recovery of the tissues from the radiation effect and gives the patient an opportunity to recover from the anemia and weakness which result from this type of therapy. There is no need to fear the loss of valuable time in employing this procedure, as mentioned by Ward.[17] A carcinoma so extensively irradiated if not destroyed will probably be inactive for this period of time.

Table III summarizes the 7 cases adequately irradiated but not hysterectomized. Four of these cases were curetted from one to three months after irradiation, and no malignant cells were found. Case 5, however, died one year later of peritoneal metastases. This demonstrates that myometrial or lymphatic invasion may be present, and curettage would not detect its presence, an observation stressed by Scheffey and Thudium.[14] There is always the possibility that a case may be more extensive than clinical findings indicate. Elton, in studying 50 removed uteri, concluded "that hysterectomy is obviously necessary for adequate evaluation of the factor of invasion." Whether removal of the uterus in this case would have prevented progression of the tumor is speculation.

Table IV groups the cases inadequately treated in our opinion and not hysterectomized. Three of the six patients who were curetted still had active disease. This group of cases were mostly in clinical Group III, two being in Group II, and one in Group IV. The survival periods definitely demonstrate the value of palliative irradiation in the inoperable group, while the end results demonstrate that clinical Group I and II carcinomas carry the highest curability rate irrespective of the grade of carcinoma.

Table V completes this group of 20 cases diagnosed at our clinic and irradiated but not operated. Cases 3 and 4 had adequate radium therapy but no x-ray. One patient in clinical Group II survived six years when she died of heart disease, while the other patient in Group II died three years later of carcinoma. The two remaining patients received palliative irradiation only.

Table VI showing the cases not verified pathologically at Mercy Hospital but referred by dependable physicians as adenocarcinomas demonstrates that the patients treated with x-ray and radium according to our technique have a higher survival rate. In Case 4, although no tissue could be obtained on curettage, the extension outside the uterus progressed rapidly.

TABLE III. SUMMARY OF CASES RADIATED BUT UTERUS NOT REMOVED

(Cases having adequate x-ray and radium)

PATIENT AGE GROUP	DIAGNOSIS ON CURETTINGS	RADIUM AND X-RAY	INTERVAL BETWEEN RADIATION AND OPERATION	OPERATION	LABORATORY REPORT	RESULT
I. C. 41 Group II	Adenocarcinoma Grade III	6,900 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	2 months	Dilatation and curettage	Necrotic endometrium No evidence of malignancy	Well and free of detectable disease 12 yr.
L. W. 71 Group II	Adenocarcinoma Grade II Papillary	6,780 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis		None	None	Living and well 6 yr. 5 mo.
E. F. 41 Group II	Adenocarcinoma Grade II Papillary	5,940 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	3 months	Dilatation and curettage	No evidence of carcinoma	Living 2 yr. Free of detectable disease
G. M. 56 Group II	Adenocarcinoma Grade II	6,000 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	None	None	None	Living 8 mo. Had early adenocarcinomatous changes polyp, 1939
M. O. 73 Group II	Adenocarcinoma Grade III	6,000 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	3 months	Dilatation and curettage	No tissue	Died one yr. later of peritoneal metastases
C. M. 64 Group III	Adenocarcinoma Grade II with areas of squamous metaplasia (adenocanthoma)	6,880 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis		None	None	No follow-up
T. R. 55 Group II	Adenocarcinoma Grade II	5,640 mg. hr. Ra. in Y-cap. 4,000 r. x-ray midpelvis	1 month	Dilatation and curettage	Radiation changes in epithelium. No definite carcinoma cells noted	Living 2 yr. 8 mo. Free of detectable disease

TABLE IV. SUMMARY OF CASES RADIATED BUT UTERUS NOT REMOVED

(Cases having inadequate x-ray and radium)

PATIENT AGE GROUP	DIAGNOSIS ON CURETTINGS	RADIUM AND X-RAY	INTERVAL BETWEEN RADIATION AND OPERATION	OPERATION	LABORATORY REPORT	RESULT
A. S. 62 Group III	Adenocarcinoma Grade III Adenocanthoma	4,200 mg. hr. Ra.El. Y-cap. 4,000 r. x-ray midpelvis	2 months	Dilatation and curettage	Very little tissue obtained. Necrotic tissue. No carcinoma	Living 5 years
M. M. E. 70 Group III	Adenocarcinoma Grade III	6,000 mg. hr. Ra.El. in st. cap. 1 sitting 4,000 r. x-ray	3 months	Dilatation and curettage	No tissue obtained	Living 4 yr. Recto-vaginal fistula
E. S. 65 Group III	Adenocarcinoma Grade III with areas of squamous metaplasia (adenocanthoma)	4,100 mg. hr. Ra.El. Y-cap. 4,000 r. x-ray midpelvis		None	None	Lived 5 yr. Developed abdominal mass
E. L. 48 Group II	Adenocarcinoma Grade III Adenocanthoma	3,850 mg. hr. Ra.El. in tubes before admission 2,000 r. x-ray midpelvis	5 months 10 months	Dilatation and curettage Dilatation and curettage	Rapidly growing adenocanthoma	Lived 2 years
E. J. E. 68 Group III	Adenocarcinoma Grade III areas of squamous metaplasia (adenocanthoma)	Radium 2 yr. and 1 yr. before admission, 6,720 in Y-cap. 4,000 r. x-ray with 200 K.V.	8 months	Dilatation and curettage	Pyometra Adenocarcinoma, Grade III	Lived 1 year
E. T. 73 Group III	Adenocarcinoma Grade III	3,120 mg. hr. Ra.El., Y cap. 4,000 r. x-ray midpelvis	5 months	Dilatation and curettage	No tissue obtained	Living 3 yr. 4 mo. free of detectable disease
A. F. 66 Group IV	Adenocarcinoma Grade II Papillary	3,000 mg. hr. straight cap. 4,000 r. x-ray midpelvis, repeated	None	None	None	Living 4 yr. 3 mo. with active disease
A. G. 53 Group II	Adenocarcinoma Grade II Papillary	4,100 mg. hr. Ra.El., Y-cap. 1,000 r. x-ray midpelvis	None	None	None	Did not finish therapy
A. M. 57 Group III	Adenocarcinoma Grade II	2,160 mg. hr. Ra.El., Y-cap. 4,000 r. x-ray midpelvis	3 months 5 months 1 year	Dilatation and curettage Dilatation and curettage Dilatation and curettage	Adenocarcinoma No evidence of carcinoma No evidence of carcinoma	Living 2 years and 2 months

TABLE V. SUMMARY OF CASES RADIATED BUT UTERUS NOT REMOVED

(Cases having incomplete treatment)

PATIENT AGE GROUP	DIAGNOSIS ON CURETTINGS	RADIUM AND X-RAY	INTERVAL BETWEEN RADIATION AND OPERATION	OPERATION	LABORATORY REPORT	RESULT
R. G. 72 Group III	Adenocarcinoma Grade II	2,400 mg. hr. Ra.El. in Y-cap. 1,500 r. x-ray midpelvis		None	None	Diabetic, stopped therapy
C. B. 67 Group IV	Adenocarcinoma Grade IV	No radium 1,600 r. x-ray midpelvis		None	None	Palliative x-ray. Lived 2 months
A. C. 57 Group II	Adenocarcinoma Grade III	7,200 mg. hr. Ra.El. in Y-cap. No x-ray		None	None	Died 6 yr. later of coronary heart disease
H. D. 56 Group II	Adenocarcinoma Grade III	6,000 mg. hr. Ra.El. in Y-cap. No x-ray		None	None	Died 3 yr. later

TABLE VI. CASES NOT VERIFIED PATHOLOGICALLY AT MERCY BUT REFERRED BY DEPENDABLE PHYSICIANS AS ADENOCARCINOMAS

PATIENT AGE GROUP	DIAGNOSIS ON CURETTINGS	RADIUM AND X-RAY	INTERVAL BETWEEN RADIATION AND OPERATION	OPERATION	LABORATORY REPORT	RESULT
R. B. 60 Group III	Adenocarcinoma	6,000 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	None	None	None	Living 10 yr. No detectable disease at this time
A. M. 58 Group III	Adenocarcinoma	6,000 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	1 year	Dilatation and curettage	Hyaline degeneration, no carcinoma	Living 4 yr. 6 mo. No detectable disease
D. M. 65 Group II	Adenocarcinoma	6,000 mg. hr. Ra.El. in Y-cap. 4,000 r. x-ray midpelvis	2 weeks	Dilatation and curettage	No evidence of carcinoma	Living 18 mo. No detectable disease
M. G. 68 Group IV	Adenocarcinoma	6,000 mg. hr. st. cap. 1 sitting before admission to Mercy 4,000 r. x-ray midpelvis	4 months	Dilatation and curettage	No carcinoma	Died 7 mo. after x-ray therapy
Sr. M. E. 55 Group III	Adenocarcinoma	2,880 mg. hr. Ra.El. in Y-cap. 9 mo. prev. 2,400 4,000 r. x-ray midpelvis	1 year	Dilatation and curettage	No tissue	Died of metastases 4 years later
M. S. 72 Group III	Adenocarcinoma	2,520 mg. hr. Y-capsule 4,000 r. x-ray midpelvis	None	Dilatation and curettage 11 mo. previous 8 x-ray Rs	Adenocarcinoma	Died of metastases 2 yr. 2 mo. after therapy
Sr. M. A. 58 Group II	Adenocarcinoma	1,300 mg. hr. 4,000 r. x-ray midpelvis	6 weeks	Total abdominal hysterectomy Bilateral salpingo-oophorectomy	Adenocarcinoma	Living 7 yr. No detectable disease at this time

If we now group all the cases adequately treated according to our standard, they number 15 of the 38 cases. These cases will be followed to determine their five-year curability rate. In the future all cases will be operated upon following the course of irradiation therapy as outlined. For, as Masson and Gregg[10] have stated, "Whether pre-operative irradiation combined with operation gives better results than operation alone will require many years to prove."

Summary

1. The technique is given for the treatment of carcinoma of the uterine fundus by combined x-ray and radium therapy, as employed at the Mercy Hospital Institute of Radiation Therapy.

2. A group of 77 proved cases of adenocarcinoma have been divided into those receiving preoperative and postoperative irradiation. The patients receiving preoperative radiation therapy are grouped clinically and graded microscopically.

3. Eleven patients receiving preoperative irradiation were hysterectomized. Five of the uteri adequately treated according to our method were free of carcinoma. Serial blocks of four of these five uteri failed to reveal residual carcinoma. The remaining 6 patients considered as inadequately treated all had active carcinoma remaining in the uterus.

4. The 27 remaining cases, irradiated but not hysterectomized, add further evidence as demonstrated by curettage or follow-up that adequate irradiation in clinical Group I or II carcinomas of the fundus has a definite value.

5. Although we cannot advocate this treatment as a substitute for surgery in patients who are good surgical risks, we feel that our plan of preoperative irradiation should be carried on until sufficient case records are on hand to determine whether the five-year salvage is greater than in cases treated by surgery and postoperative irradiation.

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Discussion

DR. HENRY L. DARNER, WASHINGTON, D. C. (By Invitation).—We have not found it possible to divide these patients into the four clinical groups suggested by the authors. The size of the uterus, the presence of any variation in consistency of the wall of the fundus and the variable degrees or complete absence of parametrial invasion have been our principal classifying factors on examination.

In our experience a tandem application, with a tube 6 cm. in length, containing 100 mg. of radium, with a wall thickness of 1 mm. gold or platinum and rubber, permitted to remain in the uterus for forty-eight hours, has usually so modified adenocarcinoma of the fundus that it cannot be recognized macroscopically or microscopically by the pathologist upon removal of the uterus, six weeks to three months after radiation. The usual exceptions are in cases where the primary site of the lesion is the apex of the fundus or where there is already myometrial or parametrial invasion.

Sterilization of epidermoid cancer of the cervix by external radiation requires from 10,000 to 18,000 r. directed over four to six ports in women under 150 pounds in weight. Above this weight external radiation is futile. Adenocarcinoma is, of course, much more resistant to radiation. Adequate irradiation of the fundus in the usual corpulent postmenopausal patient by external roentgen therapy is a most difficult problem and impossible in the average case.

The purpose of radiation therapy in the case which is amenable to hysterectomy is to sterilize the more radiosensitive elements of the tumor. This has been accomplished in our hands by intrauterine radium therapy without damage to the urinary bladder or intestines, either or both of which can be seriously affected by external roentgen therapy intensive enough to be theoretically and practically cancericidal to fundal malignancy. Fibrosclerosis of the rectum and sigmoid with attendant intractable diarrhea or more serious permanent injury and chronic irritative lesions of the bladder are frequent complications of intensive, external, roentgen therapy.

We have not found the postradiation curettage reliable as an effective means of early recognition of recurrence or failure of radiation therapy. We have all had the experience of patients with no conceivable evidence of local residual or recurrent pathology whose first evidence of recurrence is massive remote metastases.

The increased constitutional and local effects, at least in the overnourished individual, which so frequently follow adequate, external radiation will probably lead to further controversy between those who favor preoperative therapy and those who do not. We reserve intensive, external radiation for the cases in which the original and postradiation study of the patient have definitely proved persistent parametrial involvement and made postradiation hysterectomy impossible.

DR. LEWIS F. SMEAD, TOLEDO, OHIO.—I am in full accord with the recent trend toward more thorough preoperative radiation of adenocarcinoma of the uterus. All operable cases, physically fit to withstand surgery, should receive adequate preoperative radiation by x-ray or radium or by both. The best results so far obtained have been secured by this method. One might make an occasional exception in an early case, histologically classified as in Grade I or II and treat it by surgery alone or by surgery and postoperative radiation. Other exceptions might be made with operable cases classified as Grade IV or as embryonal types of carcinoma. It may be best to treat these cases by radiation alone. It is not well, however, to put too much faith in histologic classifications.

One is reminded that this subject of radiation treatment is an ever changing one when one learns that the well-established method of preoperative radiation of carcinoma of the breast recently has been discontinued in some institutions, among them the Memorial Hospital in New York. It has been discontinued because it

delayed the operation three or four months, and because it resulted in poor wound healing and other complications. I am fully aware that these same faults may be found with preoperative radiation of carcinoma of the body of the uterus.

The x-ray factors employed in the treatment of my cases of carcinoma of the uterus, and furnished me by my associates in the x-ray department, are a 400 kv. constant potential current operating a sealed x-ray tube at 5 milliamperes, a filter equivalent of 3.0 mm. of copper, a focal skin distance of 65 cm., a field size of from 250 to 400 square cm., and H.V.L. of 4.0 mm. of copper. The output is 35 r. without backscatter and 42 r. with backscatter. The depth dose at 10 cm. is nearly 50 per cent on fields above 250 square cm. Four pelvic ports are used of 250 square cm. or more in size. In a pelvis measuring 20 cm. in anteroposterior diameter the dose delivered to each port is about 2,800 r. or 11,200 r. total, measured with backscatter. This delivers about 40 per cent to the midpelvis or 4,800 r. to the tumor area. About 360 r. with backscatter are delivered to one port each day. The dose is delivered in a total of 32 daily treatments.

About two weeks after the last x-ray treatment the radium treatments are carried out. From 3,600 to 4,000 mg. hr. are given within the uterine cavity in multiple capsules filtered by 1.5 mm. platinum, and 1,600 to 2,000 mg. hr. with the same filtration plus 1 cm. of sponge rubber are applied against the cervix and vaginal vault. The latter is intended to take care of any malignancy in the cervix or vagina and to add to the general pelvic dose. The treatments are given rather slowly in two doses over a period of from eighty-nine to ninety-nine hours using only 80 mg. of radium element with heavy filtration. There is an interval of 24 hours between the two doses. The patients are usually ready for hysterectomy in from six to eight weeks after the last radium treatment.

It is felt that this method of treatment should deliver an adequate dose to the uterus and pelvis. There has not been time to check over the reports on the uteri removed at operation, but most of them have shown no remaining carcinoma on routine gross and microscopic examination. I have not found that this amount of treatment has made the hysterectomy difficult or caused poor wound healing.

DR. LEROY A. CALKINS, KANSAS CITY, KAN.—For a number of years we have proceeded on the general rule that an adenocarcinoma, whether of the body of the uterus or the cervix, required approximately twice the radiation dosage to be lethal as was required for a squamous cell carcinoma of the same size and location. Dr. Healy has recently cast doubt on this difference in susceptibility. I wonder whether Dr. Schmitz has gone far enough to be able to tell us the relative radiosensitivity of the squamous cell carcinoma and the adenocarcinoma.

DR. GEORGE F. PENDLETON, KANSAS CITY, MO.—Assuming that you have given proper intrauterine dosage and the proper roentgen crossfire through various ports are you not very much worried about the loss of the capillary bed in the parametrium after three months?

DR. SCHMITZ (closing).—It is admittedly very difficult to control the position of radium in the uterus. If you place capsules in series in a rubber tube and then pack them into the uterine cavity there is no way of telling whether they shift, nor can you determine the exact dosage you are giving at any one point. That is why the Y applicator was adopted. We are giving from 7.5 to 8 erythema doses in the uterus, which we believe is necessary to destroy the average carcinoma.

As to Dr. Smead's remark about preoperative x-ray irradiation, I believe that it has a definite place in the treatment of uterine carcinoma. I am not advocating this method of treatment for adenocarcinomas of the uterus, but I want to continue the study to evaluate this method so when forced to use irradiation on a poor operative risk, we will know which method of irradiation will give the best results.

Many reports are appearing in the literature at the present time of uteri studied after inadequate amounts of irradiation. Other investigators used from 2,000 to 3,500 mg. hours of radium in the uterine cavity and removed the uterus before a two weeks' interval. We know that the irradiation effect has not reached its maximum so quickly and therefore these studies are valueless. I do not believe that delaying the operation is a factor in recurrence if the carcinoma is thoroughly irradiated.

Replying to Dr. Calkin's question, I believe earlier impressions of the sensitivity of adenocarcinoma came from the fact that we had so few adenocarcinomas of the cervix. It was, of course, the opinion of most gynecologists and pathologists that the adenocarcinomas were more resistant than the squamous cell carcinomas. I now believe, if we had the same number of cases it would be found that the relative resistance would be about the same.

As to Dr. Pendleton's question, I do not believe that irradiation causes any disturbance of the capillary bed. I encountered no difficulty in the surgery, and there was no immediate surgical mortality and only one case with fever.

RADIUM THERAPY IN BENIGN UTERINE BLEEDING*

A Study Based on 350 Cases

A. J. Rongy, M.D., and A. D. Seley, M.D., New York, N. Y.

THE clinical study and the analysis of the results obtained in this comparatively large series of cases differs measurably from the methods commonly employed in the evaluation of the efficiency of a therapeutic agent in the treatment of disease. Ordinarily studies of a large series of cases, emanating from clinics, represent the work of a number of surgeons in both private and ward patients. The symptoms, objective and subjective, are recorded by junior members of the staff. The selection of a given procedure represents the judgment of many surgeons or frequently a standardized method of treatment. The subsequent history and final results are collated and tabulated by members of the staff, who often do not have an intimate knowledge of the medical status of the patient from the inception to the termination of the treatment.

This series of cases, covering a period of fourteen years, consists of private patients, who sought medical advice because they suffered from vaginal bleeding and associated symptoms. Each patient was first seen in the office. The medical history, the physical examination, the indication for the use of radium, the postoperative course, morbidity and complications, the subsequent history, and the final results were evaluated and carefully recorded on the history cards by the senior author.

The junior author tabulated all the facts from the records. The data obtained truly mirror the usefulness of and may serve as criteria for

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the application of radium in benign uterine bleeding. The conclusions arrived at represent an objective estimate of the effectiveness of radium for the control of bleeding in properly selected cases.

The symptoms that primarily impel these patients to seek medical advice are: (1) abnormal vaginal bleeding, (2) pain in the lower portion of the abdomen, and (3) pressure in the pelvic region. The cardinal symptom, however, is the profuse or irregular vaginal bleeding which may or may not be accompanied by pain or pressure, disturbed micturition, or other symptoms. The nature and complexity of the symptoms these patients present do not as a rule lend themselves to a standardized form of treatment. The pelvic findings, the marital and social status, the general constitution of the patient should form an all inclusive medical picture which would bespeak either for conservative or radical procedures for the control and cure of the symptoms.

The pathology underlying the disturbed vascularization of the endometrium requires further elaboration and clarification. Even microscopic study of the endometrial tissue often does not help to clarify the pathologic process, for in this series of cases a resting endometrium was found in 112, or 39.3 per cent, and a hyperplastic endometrium in 130, or 45.6 per cent, of the patients. Obviously it is difficult to explain bleeding in the presence of resting endometrium, or the existence of an endocrine imbalance without causing some changes in the endometrium. Furthermore, how does a simple curettage, which often cures the bleeding, correct an endocrine imbalance? These are puzzling problems to the clinician which require further investigation.

It is superfluous to state that no treatment of any kind should be instituted in cases of uterine bleeding before a microscopic study is made of the endometrium. It may be mere coincidence that in twelve patients in this series corpus carcinoma was discovered only after the curettings were examined. In none of these patients was malignancy suspected nor had they given symptoms which would warrant the diagnosis.

The crux of the problem in the treatment of uterine bleeding with or without fibroids is: What type of case should have the offending organ removed or when should radium be used to control the symptoms? Theoretically this should not be difficult for clinicians who are not delimited in their approach to this problem by one particular method of treatment.

The indications and contraindications for radium therapy in uterine fibroids, as enunciated by Ward,[1] will prove satisfactory in the average case. However, one is perplexed by this statement that "surgery is indicated in bleeding myomatous uteri as a general rule."

Though it is generally agreed that radium therapy is contraindicated when the uterus is enlarged to the size of more than a three months' pregnancy, actually there is no theoretical line of demarkation. The clinical findings must be evaluated in each patient, not only from the standpoint

of curing the symptoms but also as to the safety of the procedure. In the light of accumulated experience, to remove a uterus, with or without a fibroid, when a cure can be accomplished by a therapeutic agent, less dangerous and just as effective, seems not to be a rational procedure. There certainly is no justification for subjecting a middle aged woman, who is suffering from idiopathic uterine bleeding, to a major surgical operation.

We are convinced, as a result of this study, that radium is the only logical therapeutic agent in all cases of uterine bleeding not complicated by fibroids or malignancy, in women in whom childbearing is no longer a problem. Sixty-five patients in this series belong in that category and a complete cure was accomplished in all.

Uterine Bleeding Associated With Fibroids

This class of cases require greater clinical acumen correctly to decide as to the proper method of treatment. The size of the uterus, the location of the fibroids, the sensitivity of the tumor, the pain it induces, associated organic diseases, obesity, the operative risk, the sexual history of the patient, as well as the husband, should be taken into consideration before treatment is instituted.

In this series of cases complete involution of the tumor took place in 232 patients. These results definitely demonstrate the usefulness of radium in properly selected cases.

Patients suffering from submucous, pedunculated, and broad ligament fibroids, whether small or large, are never proper subjects for radium therapy. Necrosis and infection of submucous fibroids often follow radiation. When a tumor projects into the uterine cavity it is easily elicited by the curette; the uterine surface is uneven, causing a zigzagging of the curette in its up and downward movements.

Radium is definitely contraindicated in all cases of uterine bleeding in patients who give a history of having a pelvic infection or in whom pelvic adhesions may be suspected because of a previous abdominal operation. It should not be used in patients suffering from fibroids when they cause much pain and tenderness. The pain is usually caused by trophic disturbance in the tumor, which is likely to be aggravated by the radiation. The bleeding may cease but the pain remains a troublesome and annoying symptom.

Uterine Bleeding Associated With Essential Hypertension

There is a prevailing opinion among clinicians that hypertension is a contraindication for and adds to the risk of an abdominal hysterectomy. Our experience differs in this respect. Patients suffering from essential hypertension, not accompanied by myocardial disease or obesity, hardly assume an immediate additional risk in undergoing a major pelvic operation. Convalescence is seldom complicated by the hypertension; furthermore they are less subject to emboli. However, the sudden in-

duction of menopause is likely to increase further the blood pressure. Therefore it is not advisable to use radium in these patients, because of its acute effect on ovarian function, but instead perform hysterectomy without removing the ovaries, so that the patient will have the benefit of some ovarian function for one or two years.

A decision in favor of radium therapy often has to be made on the basis of the psychology underlying the sex life of the husband. Many of the husbands have reached a period of instability of their sexual powers; they are less disturbed mentally when they know that a cure can be accomplished without actually removing the genital structures, thus eliminating their apprehension that a woman who has the genital organs removed is no longer fit for sexual relationship. The average woman, too, welcomes a therapeutic measure which does not entail the removal of the uterus. She may display some anxiety about the cessation of menstruation, but she finds solace in the fact that her genital organs will remain intact. This is especially true of men and women who suffer from some imbalance of the nervous system. In this regard our experience differs from that of Flynn,[2] who maintains that highly neurotic and oversexed individuals are not suitable patients for radiation therapy. On the contrary, it has been our observation that the neurotic patient takes more kindly to a cure that can be accomplished by radium instead of hysterectomy.

Patients nearing menopause, who suffer from polyps of the cervix, form a special group for radium therapy. Usually hyperplasia of the endometrium is associated with polypoid cervical growths. These patients seldom bleed profusely, but spot and stain irregularly. The removal of the polyp should be followed by curettage, especially if the pedicle is situated high in the cervical canal. The application of a small dose of radium in these cases will not only cure the spotting and staining but will prevent future polypoid formation. The cessation of menstruation does not disturb these patients; on the contrary, they welcome it, for they no longer have to be anxious about pregnancy or resort to contraceptive measures.

The immediate constitutional reaction of intrauterine radiation is also not fully understood. The nausea, mild and severe, the flushes that often develop within forty-eight hours after the insertion of radium, can be induced only through the blood and lymphatic streams. Flushes occur because the estrogenic output is reduced. The degree of nausea usually depends upon the severity of the acidosis. How can these disturbances take place so rapidly unless the body fluids are directly affected by the radium?

Uterine Bleeding Associated With Pelvic Lacerations

Many patients who suffer from uterine bleeding require pelvic repair. Abdominal hysterectomy, without repairing the lacerated structures,

often aggravates the relaxation of the vaginal vault and not infrequently leads to its complete eversion, a most troublesome complication and extremely difficult to repair. Again, vaginal hysterectomy without reconstruction of the pelvic floor is definitely an incomplete surgical procedure. Until recently, for some reason, repair of the vaginal vault was seldom undertaken together with intrauterine radiation. It was believed that the healing power of the repaired structures would be affected by the rays. Clinical experience disproved this hypothesis. The healing process is not at all interfered with by the presence of radium in the uterus. In this series 65 patients had plastic operations on the cervix and vaginal vault. In seven the interposition operation was performed. Neither the morbidity was increased nor was the stay in the hospital prolonged. The application of radium in conjunction with repair of the vaginal vault in this group of patients proved more satisfactory than any other surgical procedure we had used heretofore in this class of cases. We believe it to be the method of choice and that it will in the future supplant other surgical procedures. Neither vaginal nor abdominal hysterectomy compares with it favorably.

It is anomalous that radium therapy is extensively practiced by radiologists. They are neither technically trained to deal with surgical procedures nor have they the necessary knowledge to evaluate properly the clinical condition of the patient. The indications and contraindications for curettage and radiation are gynecologic problems; especially is this true of patients who require supplemental surgical procedures.

We desire to emphasize briefly some of the more important items dealing with the management and results obtained in this series of cases.

Dosage

When we first instituted radium therapy in the treatment of these patients we varied the dosage from time to time and finally came to the conclusion that 1,800 mc. hr. is the appropriate dose for women aged 40 years or older. The ideal method is to insert 25 mg. in the uterus, to be left seventy-two hours, the patient thus receiving 1,800 mc. hr. of radium. Nausea and radium burns are less likely to occur when a smaller dose of radium is used over a greater number of hours.

Morbidity

Occasionally the patient will complain of crampy pain in the lower portion of the abdomen induced by the foreign body in the uterus. In 314, or 89 per cent of cases, there was no postoperative reaction. Included in these are 50 patients who had supplemental repair of the vaginal vault. Thirty-six, or 10.3 per cent, including 15 patients, who had vaginal plastics, had morbidity lasting from three to seven days. With the exception of one patient their stay in the hospital was not prolonged.

Leucorrhea

There is no doubt that intrauterine radiation increases the cervical discharge temporarily in a considerable number of patients. The necrosis of the endometrium induced by the radium often forms a thick, slimy discharge, lasting about two or three weeks, and subsides as soon as the endometrial debris is completely eliminated. The discharge, however, is not more profuse than that induced by cauterization of the cervical canal performed preliminarily or in conjunction with supravaginal hysterectomy.

Rectal Bleeding

Three patients had periodic rectal bleeding, which lasted over a period of years. No lesion in the rectum or anus was discernible. It was not accompanied by pain. The patients experienced the same sensations which they usually had preceding their normal menstruation. Clinically, it could only be interpreted as vicarious menstruation; though in one patient a proctologist was strongly suspicious of the development of an early malignancy in the upper portion of the rectum, the subsequent history of the periodicity of the bleeding confirmed the diagnosis of vicarious menstruation.

Vesical Disturbance

The severity of vesical symptoms in this series of cases was largely judged by the frequency of nocturnal micturition and how often the patient was awakened by the desire to urinate. Thirty-seven, or thirteen per cent, were definitely disturbed during day and night by the frequent desire to pass urine for many weeks following the operation. Some of these patients, however, had vaginal plastics and had to be catheterized for a number of days. In our experience, extreme vesical irritation following intrauterine radiation does not occur as frequently as is generally ascribed to it.

Menopausal Symptoms

Cessation of ovarian function, whether induced by radiation or castration, is sudden and therefore the menopausal symptoms are more acute. In the last analysis, the severity of the symptoms in normal and artificial menopause largely depends upon the compensatory constitutional adjustment of the patient. Menopausal disturbances do not differ, whether induced by radiation or castration. The belief that radiation causes more pronounced symptoms is erroneous and not confirmed by careful clinical observation. Schriener[3] and others have reached the same conclusion. Norris and Behney[4] found that the menopausal symptoms following intrauterine radiation occur in only 59 per cent of the cases. In our series, 49.7 per cent had no or only mild flushes, moderate in 40.6 per cent, and severe in 3.7 per cent. It is

interesting to note that not a single patient developed involutional melancholia during the menopausal period, though we have observed a number of such instances following hysterectomy and bilateral oophorectomy.

Involution of the Fibroid Tumor

In 232 patients, or 81.4 per cent, complete involution of the mass occurred, partial in 48, or 16.8 per cent. In a number of patients the uterus atrophied to a subnormal size. In the majority of cases hardly a trace of the fibroid could be elicited by clinical examination after eighteen months. Corscaden[5] observed "a complete disappearance of the mass in 55.8 per cent, in 28 per cent a reduction of 50 per cent or more, in 12.5 per cent a definite and important reduction."

Postradiation Pain

Many patients complained of localized pain in the lower part of the abdomen or the groins during the involutional process of the fibroid. The pain diminished and gradually subsided when the fibroid had completely or partly involuted. Clinically it is difficult to interpret the symptom of pain in the pelvic region in multiparous patients, and it is not easy to differentiate it from the specific pain induced by the involution of the fibroid. However, if upon examination the uterus is found to be sensitive or a tender spot is elicited in the region of the fibroid, it is safe to assume that the local pain is caused by the circulatory disturbance within the fibroid.

Number of Periods Following Radiation

In 197, or 56.3 per cent, the menstrual function disappeared immediately. Sixty-eight, or 19.4 per cent, menstruated once. Eighty-five, or 24.3 per cent, menstruated two or three times. One patient at the age of fifty began to menstruate regularly after a complete cessation of menstruation induced by radium twelve years before. Another patient began to menstruate after an interval of five years; she became pregnant and aborted in the third month.

Five patients, or 1.8 per cent, failed to respond to radium therapy. They continued to bleed irregularly and at times profusely. Hysterectomy finally was performed in four of the cases. Two patients required supplemental x-ray therapy, and in two others radium therapy had to be repeated. One patient, who had two applications of radium, developed carcinoma of the cervix and body of the uterus five years later. We never observed a malignancy develop as a sequel to intrauterine radiation. In this respect our experience coincides with that of W. Neill, Jr.[6]

Conclusions

1. Uterine bleeding can be cured by curettage and intrauterine insertion of radium in properly selected cases.

2. In 285 patients, the bleeding was accompanied by fibroids; in 65, no fibroids were present.

3. The average dose required to induce artificial menopause is 1,800 mc. hr. A small dose of radium is preferable to a concentrated dose.

4. Complete involution of the tumor took place in 81.4 per cent, partial involution in 16.8 per cent; not affected by the radium, 5 patients.

5. It is not advisable to use radium in patients who suffer from essential hypertension and who have no other contraindication for operation.

6. Radium is contraindicated in cases in which the uterus is enlarged to more than fourteen weeks' pregnancy. It should not be used when a submucous fibroid is suspected, nor is its use advisable in subperitoneal or broad ligament fibroids.

7. It is dangerous to use radium in patients who give a history of having had a pelvic infection.

8. The menopausal syndrome is not accentuated by radium.

9. The leucorrheal discharge is increased for a period of six to seven weeks in a goodly number of cases.

10. Sexual relationship is less likely to be disturbed following the use of radium. The libido is definitely not affected.

11. Curettage and intrauterine radiation can be safely utilized in at least 35 per cent of patients suffering from uterine bleeding. It should replace abdominal hysterectomy in 25 per cent of cases and vaginal hysterectomy in 40 per cent.

12. Curettage and radium therapy should be performed by gynecologists, not by radiologists.

The results obtained in this and other series of cases definitely show the advance made in the practice of gynecology. Broadly conceived, surgery is but an admission of the shortcomings of medical science. The greater the progress of the science of medicine, the less there will be need for surgical intervention. This is best illustrated by the therapeutic value of the recently discovered sulfa drugs. Operative procedures of the middle ear, mastoid, or empyema of the chest have been greatly reduced by their use. Similarly, intrauterine radiation, used in properly indicated cases, will reduce the operative incidence in patients suffering from uterine bleeding, with or without fibroids, in about 35 per cent of cases. A therapeutic agent which will help to reduce the morbidity and mortality in any pathologic lesion must not be ignored and should be made a part of the medical armamentarium.

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Discussion

DR. RALPH D. CAMPBELL, Madison, Wis.—There is no consensus of opinion as to radiation therapy in the treatment of uterine fibroids. The literature upon this subject is exhaustive, interesting and instructive, and indicates the greatest divergence of opinion as to the use of surgical methods and/or radiation therapy. Interestingly enough, in Europe radiation therapy takes precedence over surgery. In a symposium presented by the Chicago Gynecological Society upon this subject it was shown that leading gynecologists in that city were treating 95 per cent of all fibroids by surgery, leaving 5 per cent for radiation, which undoubtedly reflects the surgical tendency in the treatment of fibroids in this country.

The foregoing statements make Dr. Rongy's paper a most important one and certainly challenges the time-honored surgical treatment of fibroids. In the United States Howard A. Kelly and Curtis F. Burnam have treated thousands of cases successfully by radiation therapy to the exclusion of surgery.

Based upon a considerable experience, I can say that patients in, near, or past the menopause presenting large fibroids can be successfully treated by intrauterine radium.

Dr. Rongy has enumerated the well-known contraindications to the use of radium, such as age, anemias, pelvic inflammatory disease, submucous and subserous fibroids, hypertension, etc. However, I wish to point out that extreme anemia is not a contraindication to radiation, and this is especially true of intrauterine applications. In addition, the size of a tumor has been stressed by many observers as a contraindication to radiation. However, it is not the size that counts but whether or not it presents signs of degeneration.

I must re-emphasize that a diagnostic curettage is indicated in all cases to rule out intrauterine pathology and primarily carcinoma.

The essayist recommends 1,800 mc. hr. as the appropriate dosage continued over a period of three days, with which I cannot agree. Neither can I agree with his reasons for the extended dosage. It has been my practice to deliver a dose of 1,500 mc. hr. within the twenty-four-hour period with excellent results. My experience has shown a higher morbidity with the long continued dosage.

Dr. Rongy's observations upon morbidity, leucorrhea, bladder disturbances, menopausal symptoms, tumor involution and the menses are what one would expect.

It is interesting to note that the author has used radium placements at the time of plastic operations with excellent results, a procedure which I have been hesitant to do. It would seem to me that the procedure of choice would be a vaginal hysterectomy plus a complete repair.

I wholeheartedly endorse the statement that curettage and radium therapy should be performed by the gynecologist and not the radiologist.

At the University of Wisconsin we have used roentgen ray therapy with excellent results in the suitable age group as a sole agent in the treatment of many fibroid cases, naturally making the proper exclusions and not paying too much attention to the size when the tumor shows no signs of degeneration. It is common practice at the time of diagnostic curettage to decide upon a radium placement both from the standpoint of convenience to the operator and economy to the patient. Such a procedure is debatable in making a decision between the use of intrauterine radium and deep roentgen therapy. Then, too, such complications as extensive intrauterine

necrosis, infection, and obstruction and pyometra occasionally encountered in intrauterine therapy may more than offset the advantages of intrauterine radium over deep roentgen therapy.

DR. WILLIAM H. VOGT, ST. LOUIS, MO.—Occasionally I use radium for uterine bleeding and the remarks to follow are not intended to condemn the procedure. My discussion is directed chiefly toward the contraindications for its use.

We all recognize that one of the contraindications is submucous fibroids of the uterus. I do not know of any way whereby one can be certain that such a condition exists or is absent, particularly if these tumors happen to be small.

Another contraindication, which is always stressed, is pelvic inflammatory disease. If we use radium in the presence of pelvic inflammation we are likely to set up an acute process, and perhaps even a severe peritonitis. We have all operated upon patients for fibroids and then, to our surprise, encountered pelvic inflammatory disease, which we had not suspected before the operation. Because my sense of touch in gynecologic practice does not seem to be developed to that degree that I can always say that there is or is not an inflammatory disease of the adnexa present, I hesitate to use radium more frequently in the treatment of so-called benign uterine bleeding or in small fibroids. When I do use it I still do so with some fear and trepidation.

DR. JAMES E. KING, BUFFALO, N. Y.—I believe that the question of irradiation in benign disease of the uterus, or simple bleeding, should be divided into three sections: first, the hyperplasias; second, the fibroids which may be so treated; and, finally, the endometrial atrophy that gives rise to very slight bleeding and which creates a suspicion of malignancy.

So far as hyperplasia is concerned, we frequently see these cases in young women, with the exception of a few, and I think it is very wrong to do anything to castrate them. Therefore, I have always given small doses, perhaps not more than 400 millicurie hours, and usually 350. It is surprising how that will frequently afford several years of comparatively normal menstruation.

So far as fibroids are concerned, I never treat one larger than a three months' pregnancy with radium. And there again, in the bleeding occurring during the childbearing life of the woman, we are handicapped by fear of giving a large dose which might cause castration. According to my figures on the cases I reported a number of years ago there were approximately 25 per cent of my own patients that came back to me requiring a hysterectomy. How many in my series there were that were done by others I do not know, but that is not a very large percentage and I think it bears out the fact that radium is helpful in many of these fibroid uteri.

Another thing that I find divergent from Dr. Rongy's finding was the occurrence of hyperplasia in connection with these fibroids. In my series it occurred in about 70 per cent of all these fibroids. Of course, the uterus was always curetted and the pathologist is responsible for the report of about 70 to 75 per cent having hyperplasia. Therefore, when we say that the bleeding is caused by the fibroid I think that is, in the main, wrong. I think it is because these cases have a hyperplasia associated with the fibroid, and we treat the hyperplasia with the fibroid the same as we would were the fibroid not present.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—In our work we have to divide our fibroid cases into two racial groups, the Negroes and the whites. In the first we have a type of fibromyoma which appears early in life, is almost always multiple, with a great tendency to multiplication of the nodules and with a tremendous growth. In the white women we have about the same conditions that you have in the North. In the Negroes we find an almost universal association of inflammatory disease which we have to take into account when considering irradiation. We think

of the myoma in three groups, excluding the Negro group. The first is the observation group, producing no demonstrable symptoms. They are simply kept under observation, almost regardless of size, although by the time they reach a size of a four months' pregnancy they do produce symptoms. The second is the younger women in the myomectomy group, in whom the childbearing factor is essential. The third group is the hysterectomy group comprising practically all the rest.

Now we have had marked necrosis and one case of gangrene in a fibromyoma of about the size of a four months' pregnancy, following about 2,000 mc. hr. of irradiation. One was a disastrous case with the loss of the patient.

I have not had experience with the minor dosage suggested, giving 350 to 400 millicurie hours. I do not exactly see the rationality of this.

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—In an analysis of some 760 cases reported from our clinic we too decided that 1,800 mc. hr. was the ideal dose to cause a permanent cessation of the menses in a woman of menopausal age. If roentgen therapy or external irradiation is used, it takes 500 roentgens of x-ray in the midpelvis to cause the same effect and when you refer your patient to the radiologist be sure to specify the dose, otherwise she may be under- or overirradiated.

I feel that in infected cases it is very poor judgment to block the cervical canal. That brings up the question of pelvic inflammatory disease. You remember Dr. Polak's work on that subject and x-ray today is being employed routinely for inflammatory disease. We have a routine rule on our service that if a patient with radium in the uterine cavity has a temperature rise to 100.4° F. the radium is immediately removed. Then external irradiation can be continued in small dosage until you have given the desired dose without fear of spreading the infection.

The postoperative discharge following the use of radium lasts from six to eight weeks and has been so appropriately described as a "meat juice" discharge. It is very distressing to the patient and can be avoided if external irradiation is used in preference to radium.

There is a general tendency at the present time to substitute vaginal hysterectomy for radiation therapy in the treatment of benign bleedings. The argument used is that these hyperplastic cases of endometritis are potentially cases of carcinoma of the endometrium. This has not been my observation, and though surgery may have a mortality rate of only 0.5 per cent, we have no mortality rate with irradiation. The period of hospitalization is much shorter when irradiation is used and the end result is just as satisfactory.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—I have just noticed that I left out the most important group, and that is the abbreviation group, with tumors not larger than three and one-half months' pregnancy, at least not past 35, in submucous tumors associated with inflammatory disease and showing tendency to degeneration. That is probably the largest group we have.

DR. RONGY (closing).—Many of the questions raised in the discussion are fully covered in the paper, which time did not permit me to read in its entirety.

I do not wish to convey the impression that I am especially interested in the treatment of uterine bleeding with radium. I am more interested in gynecologic surgery, but these cases were selected from a large number of patients, who consulted me for uterine bleeding. I resorted to radium therapy only in patients who had contraindications for a major surgical operation or when the fibroid was so small that there could be no doubt of a favorable result.

I, too, was fearful of performing a plastic operation on the vaginal vault in conjunction with radiation. After I did one case and encountered no trouble, I followed this in all cases where such procedures were indicated. Sixty-five of these

patients had plastic operations. The healing was not interfered with, nor was the convalescence delayed, and the results on the whole were good. I believe it is an ideal method to follow in patients who suffer from uterine bleeding and require vaginal repair.

I truly believe that we have failed to take into consideration the psychologic attitude of both husband and wife in the treatment of these patients. I know of many marital tragedies resulting from the removal of the uterus and ovaries. Often the husband's attitude to his castrated wife undergoes a change when he is informed that one or more of the genital organs have been removed. Their sex life is definitely influenced by it, and it is therefore necessary in certain types of patients to conserve the organs and not remove them.

With the exception of one case, I never encountered intrauterine necrosis, infection or pyometra as a result of intrauterine radiation. If the indications are properly set the chances are these complications are not likely to occur.

Somehow, I still cannot agree with Dr. Campbell that large fibroids should be treated by intrauterine radiation. However, he is correct in stating that "generally speaking it is not the size of the tumor that counts, but whether or not it presents signs of degeneration."

The question raised by Dr. Vogt in connection with submucous fibroids is pertinent. I do, however, believe that submucous fibroids can be easily detected by the curette and that radium should never be used when submucous fibroids are suspected.

Our experience with hyperplasia of the endometrium in connection with uterine fibroids differs materially from that of Dr. King, who found this condition in 70 per cent of all his patients. This is also true of his statement that 25 per cent of his patients later required hysterectomy. Of the 350 cases we had only five failures, upon whom hysterectomy had to be performed.

I fully agree with Dr. Cooke that once infection either in the parametrium or in the genital organs is suspected, no form of radiation should be utilized.

I was glad to hear Dr. Schmitz state that he considered 1,800 mc. hr. the proper dose in this group of cases. I agree with him in his condemnation of vaginal hysterectomy as a treatment for benign uterine bleeding, instead of radiation therapy, especially when many of these patients require repair of the vaginal vault.

THE GLYCOGEN INDEX IN THE MENOPAUSE*

A Study of Certain Estrogen Functions Based on a New Method of Staining Vaginal Smears

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WITH the large number of natural and synthetic estrogen products now available commercially, there is pressing need for objective evidence of their comparative value. Attempts to fulfill this need through laboratory experiments upon spayed animals and clinical studies based upon the relief of menopausal symptoms have, for the most part, yielded evidence of only relative value. Variations in species susceptibility[1-3] to estrogens have produced a confusing array of biologic standards. Similarly, the variable and often purely psychogenic factors[4] which characterize climacteric complaints have led to interpretations which Frank[5] once described as dependent "about equally on the impressions of the physician and of the patient." Since materials for clinical use must logically be based upon human requirements and responses, the need for objective human yardsticks to take the place of clinically useless biologic standards and questionable appraisals based on symptomatic relief, is evident.

The introduction of the vaginal smear method for studying estrogenic response by Papanicolaou[6, 7] is an important contribution which, partially at least, provides the means for an objective clinical approach to this problem. A new adaptation of Papanicolaou's procedure was recently presented in a preliminary report[8] of the iodine vapor method of staining vaginal smears for glycogen. Further personal experience[9] and an independent study by Willson and Goforth[10] have substantiated the usefulness of this simple test for appraising estrogen responses. A more detailed description of this new technique, an account of its application in an investigation of vaginal glycogen in the menopause, and a study of estrogen responses to various commercial preparations are presented in this report.

The Iodine Vapor Method

The basis of this test, namely the presence of glycogen in the normal vaginal epithelium and its dependence upon estrogenic activity, is well

*Presented, by invitation, at the Fif'y-Fifth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 10 to 12, 1942.

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established.* The staining technique, moreover, is based upon a specific color reaction resulting from the well-known affinity between iodine and glycogen.† The simplicity of the staining technique, compared to the time-consuming and technically difficult procedures of Papanicolaou and Schorr, and its lack of dependence upon microscopic skill in identifying the bizarre and varied cytologic forms in vaginal smears, render this method suitable both for clinical investigation and office practice.

Technique

1. *Preparation of Smears.*—A cotton applicator is inserted into the vagina and twirled lightly (one complete rotation) against the vaginal wall. The cotton end of the applicator is then rolled lengthwise over the surface of a clean glass slide. By rolling, rather than rubbing, a uniformly thin film of cells, with minimal clumping and cell distortion, results. The film dries almost immediately and may be stained at once.

2. *Staining of Smears.*—Staining is accomplished simply by laying the slide, face down, over a shallow dish containing Lugol's solution. Iodine vapors which arise insensibly from the solution suffice to stain the glycogen-containing cells in two or three minutes. Microscopic examination may be carried out immediately. Although stains made in this manner fade in twenty-four to forty-eight hours, re-staining by the same method may be carried out repeatedly if subsequent examinations are desired. (A recent survey of smears made more than one year ago showed the same intensity of staining observed in original examinations.)

Microscopic Appearance

1. *Normal Glycogen Content.*—Vaginal smears from women with normal glycogen content are recognizable even macroscopically by the deep brown color of the stained slide. The microscopic picture shows a preponderance of large, flat, polygonal cells with rich brown cytoplasm. The unstained nuclei, recognizable as small, round, translucent bodies,

*The high glycogen content of the normal vagina during sexual maturity, its absence or diminution in menopausal and juvenile atrophy, and its close relationship to vaginal acidity have long been recognized. The dependence of normal glycogen values upon ovarian function and the ability of estrogen therapy to restore these values in the atrophic and glycopenic vaginal mucosa, have been conclusively demonstrated as a result of many investigations, notably those of Lewis,[11, 12] Cruikshank and Sharman,[13] Davis,[14, 15] Adair and Hesseltine,[16] Cotte, Mileff and Meyer,[17] and McLaren.[18] These studies were based upon histologic examinations of tissues obtained post mortem and by biopsy and stained for glycogen by the usual histochemical methods. Herrnberger and Horstmann[19] by staining vaginal smears of children with Best's carmine method, were able to demonstrate an increase in intracellular glycogen following the oral administration of estradiol benzoate. A good summary of the literature pertaining to vaginal glycogen is contained in their publication.

†The well-known affinity between iodine and glycogen has long been employed in histologic methods (Langhans, 1890). Merkel[20] recommended dilute Lugol's solution as a means of detecting vaginal epithelial cells in medicolegal investigations. He described the chocolate-brown or terra cotta color of the glycogen-rich vaginal cells which differentiates them from epithelial elements from other parts of the body. Schroeder, Hinrichs and Kessler[21] confirmed Merkel's description in their studies of vaginal glycogen as related to bacterial flora and vaginal acidity. Both Merkel and Schroeder noted variations in glycogen content as well as occasional complete absence, in instances of "vaginitis." Mathes,[22] according to Schroeder, utilized iodine in crude colorimetric determinations of vaginal glycogen by irrigating the vagina with Pregyl's solution. Schroeder, Hinrichs and Kessler attempted more accurate colorimetric studies by comparing the color reactions obtained (from the addition of one drop of Lugol's solution to a given quantity of diluted vaginal secretion) with a color chart representing reactions to specific amounts of pure glycogen in solution. Krumm[23] and Palmer[24] advocated the use of Schiller's iodine test for carcinoma (which depends upon the absence of glycogen in areas suspected of malignancy) as a means of determining the "absence of the follicular secretion."

The iodine vapor method was a chance discovery while investigating the possibilities of Merkel's technique in determinations of estrogen states from vaginal smears.

are located in the central portion of the cells. Varying numbers of smaller and more rounded epithelial cells taking a deep brown color are also found with some degree of regularity. In contrast to the idiophilic brown cells, a large number of nonglycogenic, unstained or lightly stained lemon-yellow cells of irregular size and shape and with poorly defined borders, make up the balance of the picture. Variations in the proportion of iodophilic and non-iodophilic cells have been observed during various phases of the normal cycle, although an exact relationship has not as yet been determined. The greatest number of deeply stained iodophilic cells has been observed during the follicular phase.

2. *Glycogen Deficiency (Glycopenia).*—Smears from women during various stages of the menopause as well as from children prior to puberty are distinguishable macroscopically by the absence of the rich brown color of the stained smear. Such slides have a lemon-yellow, buff, brownish-yellow, or light brown appearance, depending upon the degree of glycogen poverty. In extreme grades of vaginal atrophy, as in very young children, or in advanced stages of the menopause, smears consist almost entirely of amorphous cellular debris and varying numbers of yellow squamous cells; small round cells (''deep cells'') are also present. In less advanced stages of ovarian hypofunction (as in earlier phases of the menopause and in prepubescent children) glycogen deficiency is discernible by the presence of mottled cells, i.e., cells containing small, irregularly distributed brown deposits at the cell margins and in the cytoplasm. The brown color rarely involves the entire cell as in sexual maturity. The few cells which stain diffusely are smaller than normal and stain less intensely than in high estrogen states. Unstained, irregularly shaped cells, typical of the superficial layer, are also present in abundance. In early stages of the menopause, smears indistinguishable from the normal are observed frequently.

Grading of Smears

The following system of grading, based on glycogen content and intracellular distribution, is proposed for classifying smears stained by the iodine vapor technique. A somewhat similar scheme, based on the proportions of iodophilic and noniodophilic cells, was employed by Willson and Goforth.*

Grade I.—Complete glycopenia. Smears of this type contain only small yellow cells of varying sizes and shapes and large amounts of amorphous cellular debris. In extreme degrees there is marked paucity of epithelial elements (Fig. 1).

Grade II.—This grade is marked by a greater abundance of epithelial elements than Grade I. Iodine vapor staining depicts glycogen in irregular brown deposits at the cell margins or scattered irregularly throughout the cytoplasm (''mottled cells''). Diffusely stained brown cells, usually of the small round variety (''deep cells'') may also be present in small numbers. Many glycopenic yellow cells are also present (Fig. 2).

Grade III.—A further increase in cell numbers is evident in this grade as compared to the preceding. The cells are larger and more regular. The diffusely stained cytoplasm has a light brown color. Noniodophilic yellow cells are also present in abundance (Fig. 3).

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* +, only an occasional glycogen-containing cell.
++, less than one-third of the cells contain glycogen.
+++, from one-third to two-thirds of the cells contain glycogen.
++++, more than two-thirds of the cells contain glycogen.

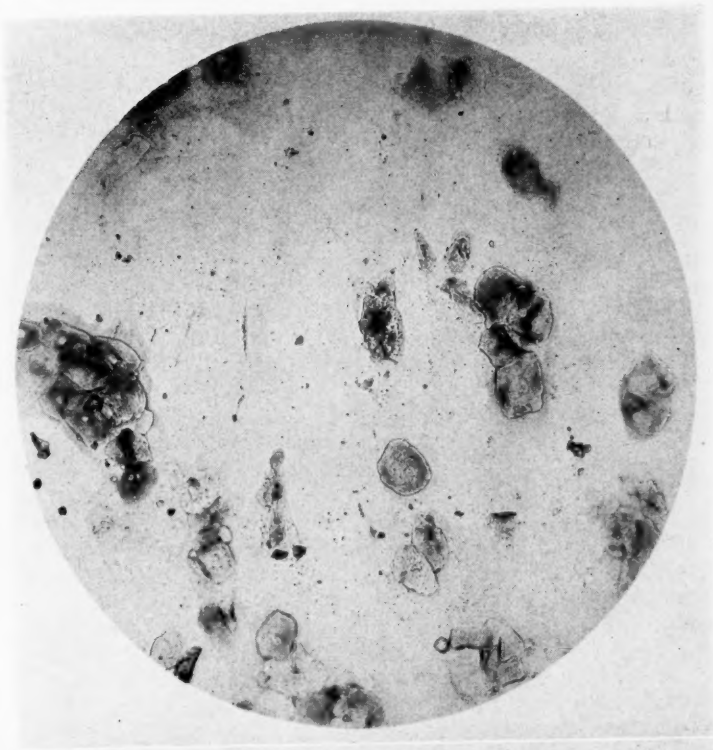

Fig. 2.

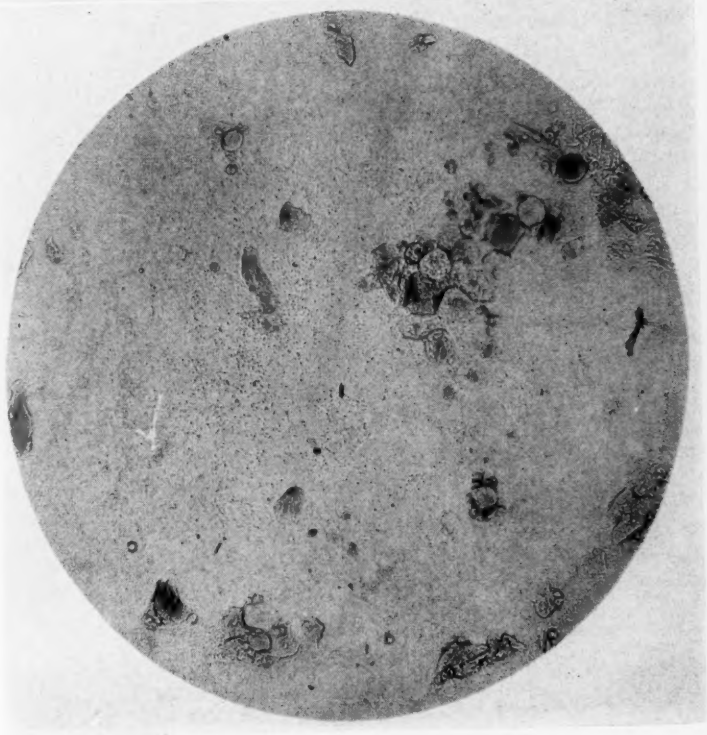

Fig. 1.

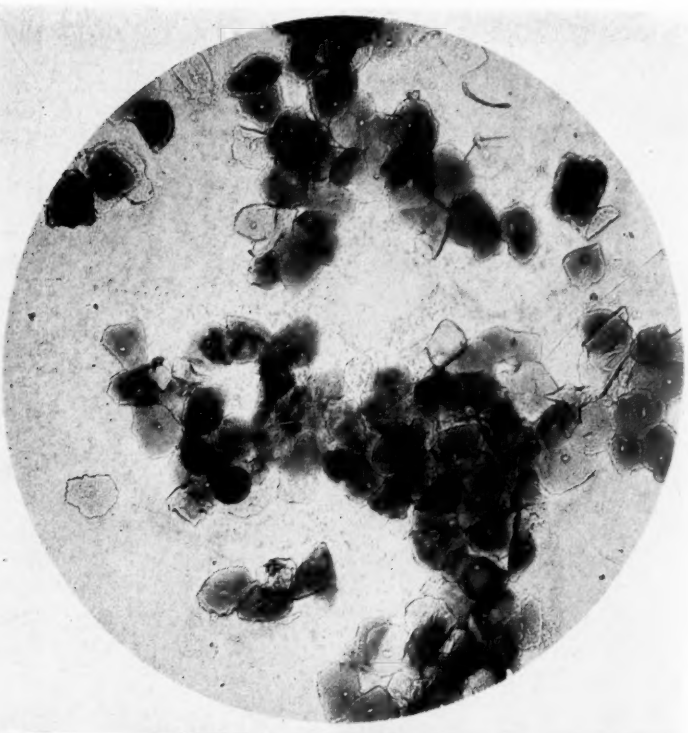

Fig. 4.

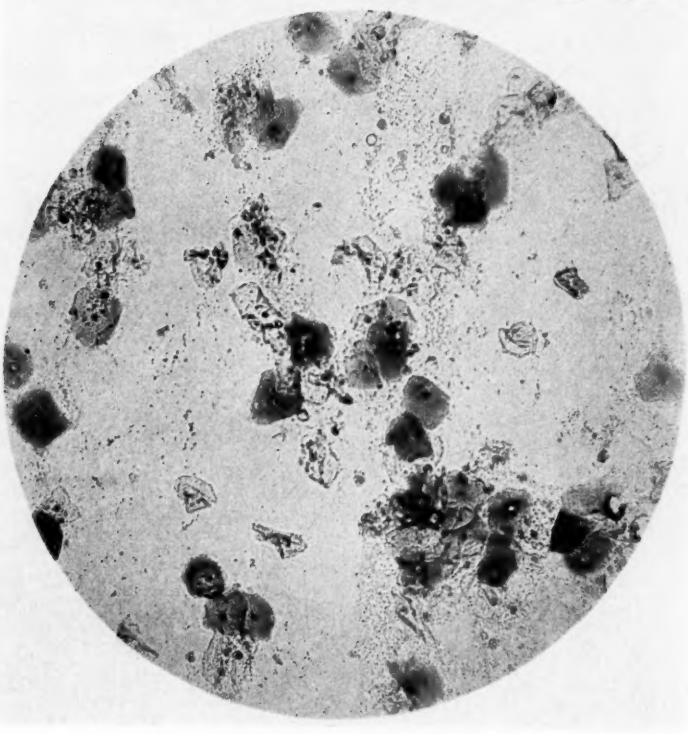

Fig. 3.

Grade IV.—This grade is easily recognized by the presence, almost exclusively, of large, flat, deeply stained brown iodophilic cells, present singly or in large clumps. This grade represents maximal estrogenic effect and corresponds to the smear of the normal proliferative or follicular phase (Fig. 4).

The Vaginal Glycogen Index of Estrogenic Activity in the Menopause

Studies of the menopausal state within recent years have repeatedly indicated that cessation of the menses is not accompanied abruptly by a disappearance of estrogens. Continued elaboration by the ovaries or other endocrine organs, such as the adrenals, or the action of estrus-inducing agents derived from extrinsic sources (food), have been suggested as reasons for postmenopausal persistence of estrogens in the blood and urine,[25-27] postclimacteric endometrial hyperplasia,[28] normal vaginal smear pictures,[18, 29] and varying amounts of vaginal glycogen[18, 19] after the natural and artificial menopause. According to Salmon and Frank,[29] only 40 per cent of postmenopausal smears gave negative evidence of estrogenic function. McLaren's study[18] showed normal smears in 78 per cent and led to the conclusion, also reached by Bennett and TeLinde,[30] that vaginal smears have no value as guides to estrogenic therapy as claimed by Papanicolaou and Schorr.[7]

To determine whether smears stained for glycogen by the iodine vapor method gave similar evidence of residual estrogenic activity, studies were made of 130 postmenopausal women with chronic, nonfebrile diseases and ranging in age from 33 to 97 years. With the exception of 22 (16.9 per cent) whose menopause had been induced by irradiation or surgical castration, the remaining 108 entered the climacteric spontaneously. Of the latter, 21 were able to give reliable information as to the last date of menstruation. Vaginal smears, after iodine vapor staining, were graded according to the system described above. The results are summarized in Tables I to III.

TABLE I. DISTRIBUTION OF GLYCOGEN GRADES IN NATURAL MENOPAUSE ACCORDING TO AGE IN 108 WOMEN

AGE	GRADE I	GRADE II	GRADE III	GRADE IV
100				
95		1		
90	2	1		
85	3	2	2	
80	1	6	2	
75	4	3	4	1
70	3	12	1	
65	4	5	5	1
60	2	5	3	
55	1	6	3	1
50	2	5	6	
45	2	1	4	
40		1	3	
Total	24	48	33	3
Per cent	22.2	44.4	30.6	2.8

TABLE II. AGE DISTRIBUTION OF GLYCOGEN GRADES IN ARTIFICIAL MENOPAUSE AND NATURAL MENOPAUSE OF KNOWN DURATION

AGE	NATURAL MENOPAUSE (21)				ARTIFICIAL MENOPAUSE (22)			
	GRADE I	GRADE II	GRADE III	GRADE IV	GRADE I	GRADE II	GRADE III	GRADE IV
75	2							
70	1	1						
65	2				1			
60	1	2	2					
55	1	2	1				1	
50			2			4		
45	1	1				3	1	
40			2		2	6	1	
35						1		
30					1	1		
Total	8	6	7		4	15	3	
Per cent	38.0	28.7	33.3		18.1	68.1	13.6	

TABLE III. DISTRIBUTION OF GRADES ACCORDING TO DURATION OF MENOPAUSE

YEARS OF MENOPAUSE	NATURAL MENOPAUSE				ARTIFICIAL MENOPAUSE			
	I	II	III	IV	I	II	III	IV
35-40	2							
30-35	2							
25-30	1							
20-25	1	1						
15-20	1	1	1			1		
10-15		2			1	3		
5-10	1	2	3		1	3	1	
1- 5			3		2	8	2	
Total	8	6	7		4	15	3	
Per cent	38	29.7	33.3		18.2	68.2	13.6	

Table I shows the distribution of the four glycogen grades *according to age* in 108 women with natural menopause. Table II compared the grade distributions (according to age) in the 22 women with artificial menopause to the 21 subjects with natural menopause of known duration. Table III compares the distribution of the four grades *according to years of duration* in natural and artificial menopause.

Discussion

Analysis of the data presented in Tables I to III shows that glycogen in variable amounts is found in all age groups of menopausal women regardless of whether the climacteric was spontaneous or induced. Complete absence of all traces (Grade I) was noted in 21.5 per cent *of the entire series of 130 patients, including both natural and artificially induced menopause* (108 patients in Table I plus 22 with artificial menopause in Table II). Advanced glycopenia, but with minimal traces of glycogen (Grade II) was present in 48.4 per cent of the combined series; moderate deficiency, or, from the other point of view, moderate estrogen stimulation, as shown in Grade III, was present in 27.6 per cent. Evidence of apparent estrogen *sufficiency,* as indicated by Grade IV smears, was present in 3 patients (2.3 per cent), aged 57, 63, and 71 years, re-

spectively, who had entered the menopause spontaneously. Glycopenia, indicative of advanced or complete estrogen *deficiency* (Grades I and II) was thus present in approximately 70 per cent, whereas evidence of moderate and approximately normal vaginal stimulation (Grades III and IV) was present in 30 per cent. The discrepancy between these findings and those indicated by Salmon and Frank and by McLaren, seems to indicate that the glycogen index may be a more sensitive indicator of estrogenic activity than cell morphology. Willson and Goforth's study also showed that glycogen increase preceded change in cell types in their investigations of the effects of stilbestrol on the vaginal mucosa, as determined by the iodine vapor technique.

Table II shows a similar proportion in the group of women with natural menopause of known duration: Moderate stimulation, 33.3 per cent; estrogen deficiency, 66.6 per cent. The group with artificially induced climacteric, on the other hand, showed moderate estrogen stimulation in only 13.6 per cent and advanced and complete glycopenia in 86.2 per cent. While the series is too small to admit sweeping conclusions, there is apparent evidence to indicate that postmenopausal estrogen stimulation, which normally persists for some time after the natural menopause, is reduced by castration. This would seem to show that the ovary is the chief source of estrogen elaboration after the menopause. Possible extraovarian sources of estrogen are indicated by the persistence of moderate stimulation in 13.6 per cent.

The probable primary importance of the ovary as the source of postmenopausal estrogen stimulation is shown (Table III) also by the fact that Grade III reactions were observed as late as twenty years after the natural menopause, whereas the same degree of estrogen stimulation was present no longer than ten years after castration.

Further studies with larger series of castrates and women with natural menopause of known duration are necessary to provide precise data. The simplicity of the iodine vapor technique makes it suitable for such studies in institutions where appropriate material is available.

Glycopenia in Vaginitis and Febrile Conditions

While Adair and Hesseltine[16] noted increases in vaginal glycogen following the local administration of lactose in senile vaginitis and vaginal trichomoniasis, the recent study of Willson and Goforth indicates that excess of ingested carbohydrate does not influence the glycogen content of women with postmenopausal glycopenic vaginal atrophy. The promptness, however, with which Willson and Goforth were able to induce glycogen increases by the administration of estrogen, regardless of carbohydrate intake and often before changes in cell morphology could be recognized by the Schorr technique,[31] is further evidence that the glycogen index is a sensitive indicator of estrogenic activity.

While the *absence* of glycogen in the vaginal epithelium is generally accepted as evidence of estrogenic deficiency, the possible effects of concomitant disease, constitutional defect, or local disorders preventing the mobilization of glycogen by estrogens must also be recognized. The findings of earlier writers[32-34] that glycogen poverty is frequently associated with tuberculosis, chlorosis, hyperthyroidism, asthenic habitus, and infantilism is augmented clinically by the well-known association of menstrual disorders[35] and vaginitis[36] in women with debilitating conditions. Sharp and Mack[37] have similarly shown a frequent association of hemopoietic phenomena and endocrine disorders in women. The general assumption in most clinical discussions of these relationships is that ovarian function (i.e., estrogen elaboration) is suppressed by the concomitant disease. The fact, however, that purely local infections of the vagina (such as *Trichomonas vaginalis* vaginitis) are often associated with glycogen poverty in the presence of normal menstrual function, suggests the presence of local or general "antihormonal" factors, rather than primary ovarian failure, as causes of estrogen deficiency and glycopenia in certain instances.

This explanation was strongly suggested by our observation that vaginal glycopenia in sexually mature tuberculous women was present only during the febrile and rapidly deteriorating phases of the disease. When the disease was arrested or stationary, normal glycogen values were consistently present. Women with normal glycogen smears at the onset of the disease frequently became completely glycopenic in the terminal, highly febrile stages. Our investigations[9] with estrone administrations to menopausal tuberculous women, furthermore, showed progressive diminution of vaginal glycogen response as the patient's clinical status deteriorated. This decline was invariably accompanied by fever. One patient (a surgical castrate), with rapidly progressive generalized tuberculosis, remained completely refractory to large doses of estrone administered orally as well as parenterally over a period of five weeks. Daily vaginal smears and post-mortem histologic examination of the vaginal mucosa revealed complete lack of glycogen. Another patient, studied at intervals over a period of nine months, was remarkably "estrogen sensitive" until the last month when, during the terminal febrile phase of her disease, she showed progressive loss of response to identical doses. Herrnberger and Horstmann similarly noted abrupt cessation of glycogen response to the administration of estradiol benzoate with the development of intercurrent pneumonia in a previously estrogen sensitive child. Our observations and those of Herrnberger and Horstmann[19] indicate that some toxic factor, such as fever, may prevent the metabolic activity of estrogen or actually cause its destruction. This interpretation, rather than that of ovarian inhibition, would seem to offer an explanation of the occurrence of amenorrhea and vaginal glycopenia in some wasting diseases.

From the evidence cited above, it would appear that successful replacement therapy with estrogens should not be expected in febrile states. Moreover, it seems possible that many instances of nonspecific vaginitis may have their origins in glycogen poverty and consequent lowered resistance to ordinary bacterial invaders as a result not only of primary ovarian deficiency, but also of febrile states or local agents which counteract estrogenic functions. Finally, the importance of eliminating subjects with febrile conditions and vaginitis, when utilizing the vaginal glycogen index in assay studies, must be emphasized.

The Vaginal Glycogen Index as a Basis for Human Assay

The lack of vaginal atrophy as well as glycopenia in the early, symptom-producing phases of the menopause in most women, indicates the limited clinical value of vaginal smear methods as guides to symptomatic treatment. The sensitivity of the vagina to small amounts of estrogen, however, and the ease with which the vaginal glycogen response can be visualized by the iodine vapor technique, suggest the usefulness of this method of approach in controlling therapy of senile and juvenile vaginitis as well as in determinations of the relative potencies of various commercial estrogens as judged by their effect upon menopausal women with advanced glycopenic vaginal atrophy. Applications of this procedure in studies of oral, parenteral and vaginal administrations of estrone, as well as of stilbestrol, have already been reported.[9, 10]

The present study includes: (a) Determinations of estrone responses with amounts commonly employed in parenteral therapy; (b) comparisons of reactions to identical amounts of estrone administered by the oral and vaginal routes; (c) comparisons of glycogen responses to identical amounts of estrone, estriol, alpha-estradiol, diethyl-stilbestrol, sodium estrone sulphate, and estrone-estriol mixture when given by the oral route.*

(a) *Estrone by Injection* (Fig. 5, *A*).—Two postmenopausal subjects (G. M., aged 72 years; B. V., aged 81 years) received 3.0 and 6.0 mg. of crystalline estrone, respectively, given in three equal injections at four-day intervals. The smaller amount was administered in three injections of 1.0 mg. crystalline estrone dissolved in oil (10,000 i.e.); the larger amount was given in three injections of 2.0 mg. of crystalline estrone in aqueous suspension. The resulting vaginal glycogen responses (as determined from daily vaginal smears), when plotted graphically, give practically identical curves. The smaller dose (3.0 mg.) produced a maximal reaction (Grade IV) on the eleventh day after the onset of treatment and maintained this effect for five days. The larger amount (6.0 mg.) produced its maximal response on the tenth day and sustained

*The estrogen preparations employed in this study were supplied as follows: Estrone, estriol, estrone-estriol mixture by Parke, Davis and Co., Detroit, Michigan. Alpha-Estradiol by Roche Organon Inc., Nutley, N. J. Diethylstilbestrol and Sodium estrone sulfate by Ayerst, McKenna and Harrison, Rouses Pointe, N. Y.

this level for eight days. Return to pre-treatment grades occurred at approximately the same time (twenty-one days).

(b) *Estrone by Oral and Vaginal Routes* (Fig. 5, *B, C, D*).—Two subjects (M. P., aged 44 years; M. T., aged 66 years) received a total of 9.0 and 15.0 mg. of crystalline estrone, respectively, in 6 and 10 daily oral doses of 1.5 mg. each. Vaginal glycogen responses were closely similar. Maximal effects (Grade IV) were obtained in each instance on the seventh day. This effect was maintained eight days following the smaller (9.0 mg.) and fifteen days after the larger (15.0 mg.) amount.

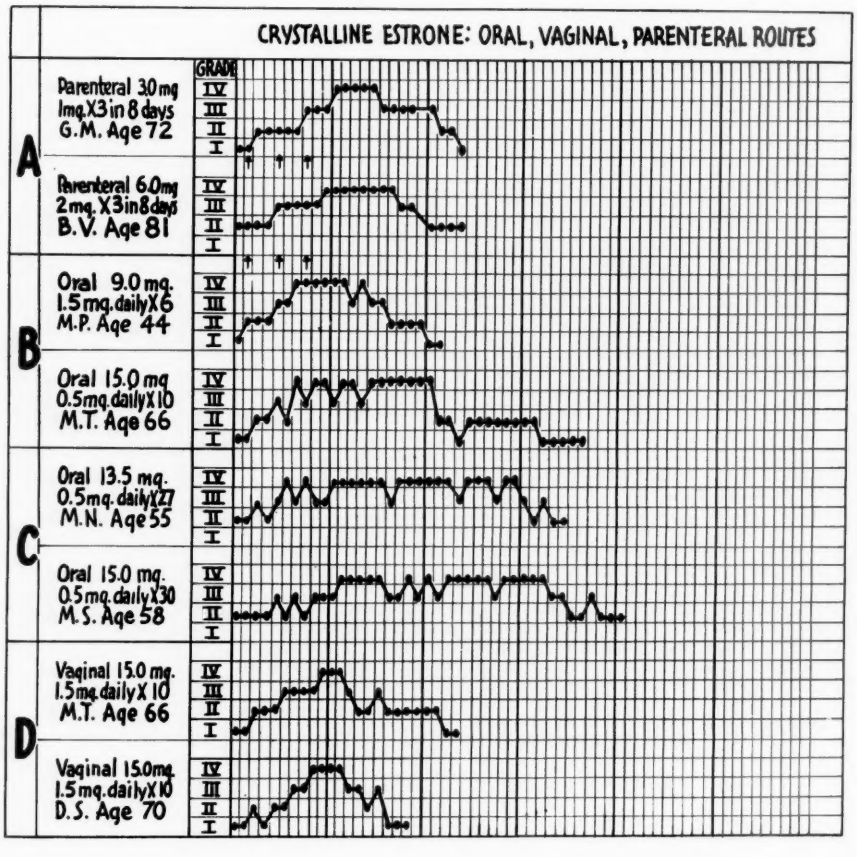

Fig. 5.

Two subjects (M. S., aged fifty-eight years; M. N., aged 55 years) were given 0.5 mg. of crystalline estrone orally for twenty-seven and thirty days, respectively. The corresponding curves again showed striking similarity. Sustained maximal effects (Grade IV) were obtained in each instance on the eleventh day and were maintained throughout the course of treatment with only minor fluctuations. Return to the pre-treatment grades became evident four days after cessation of treatment.

Two subjects (M. T., aged 66 years; D. S., aged 70 years) were each given 15.0 mg. of crystalline estrone in 10 equal daily doses (1.5 mg.

each) for ten days by the vaginal route. A striking similarity of the resulting curves is evident. Maximal effects appeared on the ninth and tenth days and were maintained for three and four days, respectively. Return to the pre-treatment states occurred on the nineteenth and twenty-third days. One of these subjects (M. T.) had previously received the same dosage by mouth. Comparison of the vaginal glycogen curve, following oral administration (see above), and the curve after vaginal administration, shows a similar though more sustained reaction from oral administration of the same amount.

(c) *Estrone, Estriol, Estradiol, Stilbestrol, Sodium Estrone Sulfate, and Estrone-Estriol Mixture by Oral Administration* (Figs. 9 and 11).—Eighteen subjects (three for each of the above-named preparations) received totals of 10 mg. of estrone, estriol, estradiol, stilbestrol, and estrone-estriol mixture, respectively, in 1.0 mg. doses for a period of ten days; the sodium estrone sulfate preparation (supplied in 1.25 mg. tablets) was given daily for eight days (total 10.0 mg.). Three additional women of the same age range (age 66, 72, 81) each received 1 gr. of desiccated thyroid (U.S.P.) daily for ten days to serve as controls. No change in the vaginal glycogen content was observed from daily vaginal smears in the control group, whereas all who received the oral estrogen products showed readily demonstrable, though quantitatively variable, responses. No toxic side-effects were noted in any of the 18 women receiving estrogen therapy.

Estrone.—One milligram doses of crystalline estrone dissolved in corn oil produced typical responses noted in the previous studies. Maximal (Grade IV) reactions were observed in two patients (Cases 5 and 27) on the eighth and sixth days of treatment, respectively; Patient 7, a less sensitive subject, attained only a Grade III reaction on the ninth day (Fig. 6).

Estriol.—One milligram doses of estriol uniformly showed a less pronounced estrogenic action than identical amounts of estrone by mouth. The maximal reactions obtained were Grade III, indicative of only moderate estrogenic effect (Cases 12 and 14); this grade was attained in six to nine days and was maintained, respectively, for five and six days. Patient 13, who had a Grade III reaction at the onset of therapy, reached a Grade IV effect in five days and maintained this stimulation for eight days (Fig. 7).

Estrone-Estriol Mixture.—A preparation containing 0.5 mg. each of estrone and estriol was given daily for ten days. Grade IV responses were obtained in all three subjects and were maintained steadily for two, five, and nine days, respectively. The resulting curve closely stimulates that for estrone, and indicates a greater potency than that of estriol in the same amount (1.0 mg.) (Fig. 8).

Alpha-Estradiol.—One milligram doses daily for ten days produced a maximal effect in all three subjects on the tenth, eleventh, and twelfth days, respectively. Grade IV reactions were sustained from two to six days. Except for variations in sustaining reaction, the effect compares closely to that obtained with identical amounts of estrone (Fig. 9).

Diethylstilbestrol.—One milligram doses daily for ten days produced maximal effects in all three subjects in four to nine days though maintenance at an even level (as with estrone and estradiol) was not obtained in any instance (Fig. 10).

Sodium Estrone Sulfate.—One and one-fourth milligram doses daily for eight days (total 10.0 mg.) produced a maximal (Grade IV) reaction

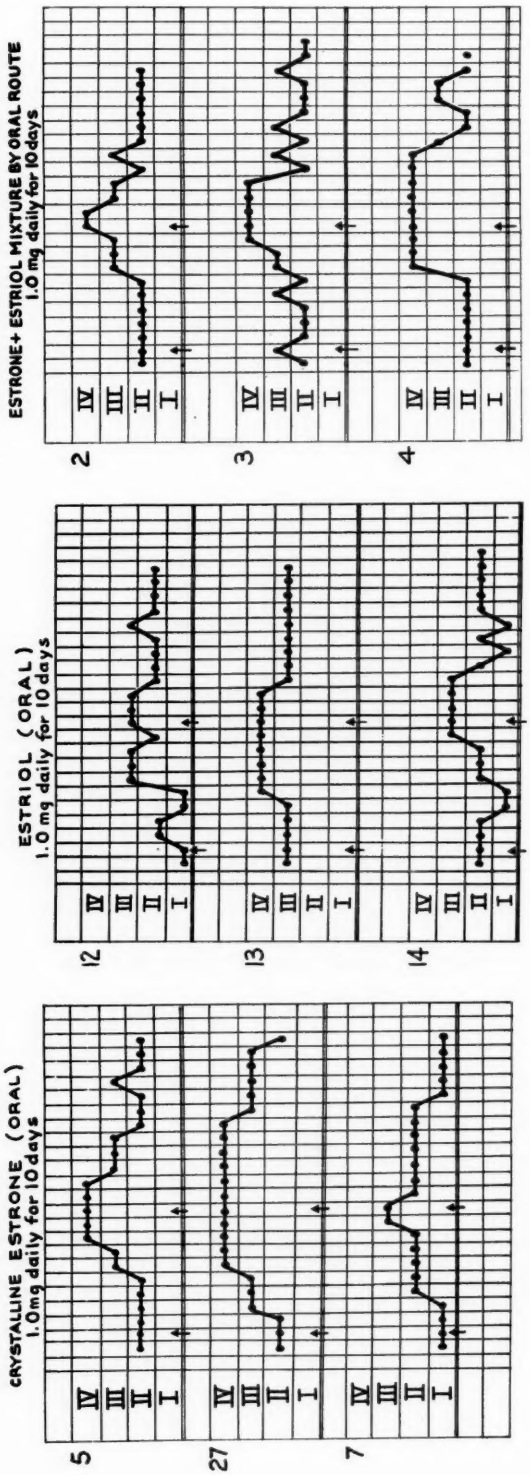

Fig. 6.

Fig. 7.

Fig. 8.

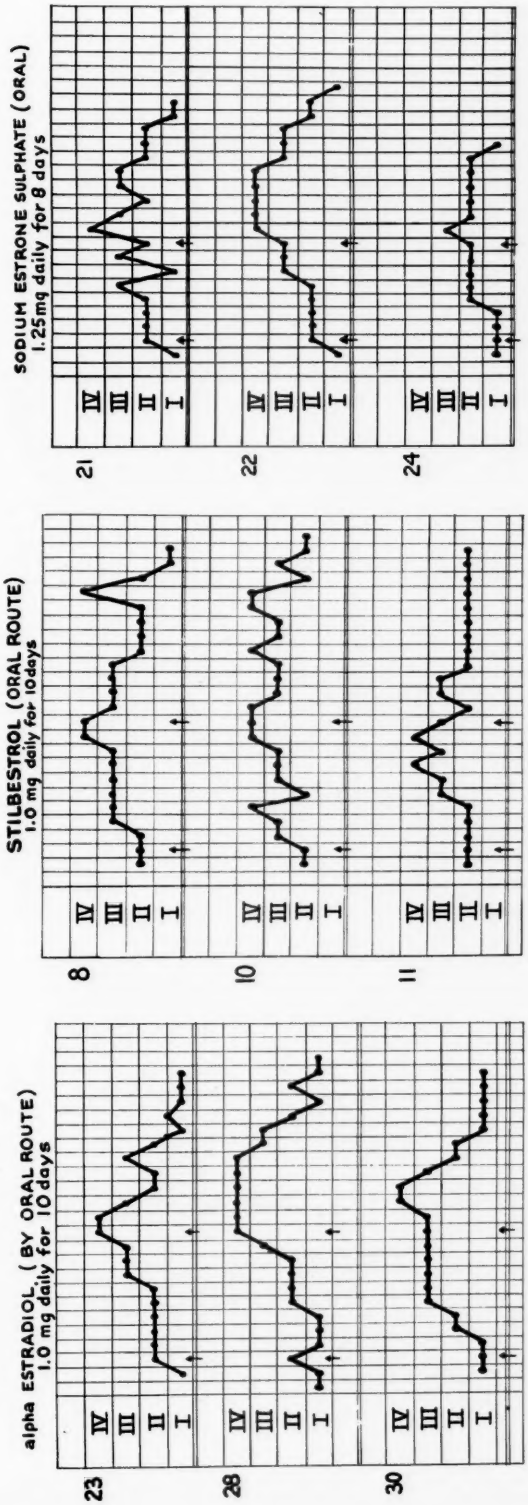

Fig. 9.

Fig. 10.

Fig. 11.

in two of three subjects on the ninth day; the third subject attained only a Grade III reaction on the ninth day. A sustained maximal effect of five days was obtained only in one instance (Case 22) (Fig. 11).

Discussion

The striking uniformity of the vaginal glycogen response to estrone by the parenteral, vaginal and oral routes of administration, also shown in previous studies[8, 9] would seem to recommend this substance as the basis for comparisons of other estrogens in human potency determinations. However, until the minimum amount of estrone capable of producing and sustaining a maximal (Grade IV) reaction has been determined, comparisons must be limited to the effects obtained with identical weighed amounts, arbitrarily chosen.

Determinations by the glycogen index have thus far indicated that the minimal effective dose of estrone capable of producing and maintaining a maximal reaction ten days is probably less than 3.0 mg. when administered by injection and less than 5.0 mg. when given by the oral route. Further fractionation of dosage is necessary to determine these limits.

Our investigations have indicated further that oral administration generally seems to evoke a more prompt, parenteral administration, a more prolonged reaction. Moreover, we have shown also that daily divided dosage, exerted a more prolonged effect when given by mouth, than identical total amounts ingested at once.[9] Besides the striking demonstration that estrone (contrary to general belief) is highly effective by the oral route, our glycogen determinations also show the apparent superiority of this route to vaginal administration.

Due to increasing interest in oral estrogen therapy and the evident need of a standardization procedure employing the human subject, we were encouraged to apply the iodine vapor technique in a comparative study of various other estrogen preparations. From these studies (Figs. 6 to 11), the weak estrogenic activity of estriol as compared to estrone given orally is immediately apparent. Alpha-estradiol, on the other hand, compares favorably with estrone, whereas stilbestrol, a synthetic estrogen, in equal amounts exerted a prompt though poorly sustained glycogen response. Ferin[38] has also noted this irregular response to stilbestrol in vaginal smear studies comparing this substance to natural estrogens. The apparent near equality of estrone and stilbestrol in estrogenic potency (when compared in equal oral dosage) is significant in the light of previous estimates by other methods, that oral stilbestrol is from 2.5 to 25 times more active than estrone by injection.[39, 40] Sodium estrone sulfate, while giving evidence of strong estrogenic action, manifested marked variation in the glycogen responses in the trials thus far completed. Further tests of this substance are necessary to determine its comparative value. Estrone-estriol mixture (0.5 mg. of each in oil)

produced an effect comparable to that obtained with 0.5 mg. of estrone alone, an observation which is contrary to the belief of Sevringhaus[41] that "mixed estrogens known now as estrogenic substances, and estriol glucuronide appear to have an advantage per unit over the pure estrone, which is the chief constituent of the mixture."

Further fractionation of dosage is necessary to determine the minimum effective dose of each of these oral preparations. From the strikingly uniform responses obtained with oral estrone, it would appear that this substance can serve as the standard of oral estrogenic activity in the human test in the same manner as its characteristic reaction in animals has been made the basis of biologic assay methods.

Summary

The iodine vapor method of staining vaginal smears is presented as a rapid and simple means for determining the specific glycogen response to estrogen activity in the human subject. This method of clinical investigation is based upon observations that normal vaginal glycogen content parallels estrogen sufficiency, whereas diminution of glycogen (glycopenia) is indicative of estrogen deficiency.

To determine the incidence of glycogen poverty in postmenopausal women, vaginal smears from 130 climacteric women (after staining by the iodine vapor procedure) were graded according to glycogen content. The incidence of the four glycogen grades was calculated according to age, duration of the menopause, and the nature of the climacteric, whether spontaneous or artificially induced. The significance of the findings, in terms of other reports of postmenopausal estrogen elaboration, is discussed. The possible "anti-hormonal" effects of various systemic and local disorders (febrile states and vaginitis) upon estrogenic activity, are suggested by observations in tuberculous women.

Experience to date has established the usefulness of the glycogen index in estimating therapeutic response of estrogen therapy in juvenile gonorrheal and senile atrophic vaginitis. Evidence of its further value as a simple and sensitive indicator of estrogen activity in human subjects is presented in potency determinations of several commercial products.

Conclusions

1. The iodine vapor method of staining vaginal smears for glycogen provides a sensitive index of human estrogenic activity.

2. The persistence of variable amounts of vaginal glycogen in menopausal women provides additional evidence of continued estrogen elaboration by the ovary or from extragenital sources.

3. Although ovarian deficiency is the chief cause of vaginal glycopenia, possible "antihormonal" factors present in local and systemic disorders may be responsible for glycogen poverty, especially that observed in certain wasting diseases during sexual maturity.

4. The clinical usefulness of vaginal smear methods (including the glycogen index) is at present limited largely to the control of estrogen therapy in vaginitis and to clinical investigations of estrogen potencies in suitable human subjects with advanced menopausal atrophy.

5. Experience with the glycogen index as a method for the comparative evaluation of estrogens in the human subject permits the following tentative deductions:

(a) Estriol, hitherto considered superior to estrone for oral medication on the basis of animal experiments, is less effective in the human than an equal weight of estrone.

(b) Alpha-estradiol, given as oral tablets, produces an estrogenic effect comparable to that induced by an equal weight of estrone in oil.

(c) Diethylstilbestrol in oil solution produces a more rapid glycogen effect when given by mouth than equal weights of estrone and alpha-estradiol. The glycogen response to stilbestrol fluctuates widely in comparison to the uniform effect obtained with estrone and alpha-estradiol.

(d) An estrone-estriol mixture (0.5 mg. of each in oil solution) orally, produces a glycogen reaction curve comparable to that induced by 0.5 mg. doses of estrone alone.

(e) Estrone produces uniform response and maintenance by all routes of administration, and can serve as a standard for comparative assays of estrogens in the human subject.

I wish to express my indebtedness to Dr. Henry Spitzer for valuable assistance in obtaining daily vaginal smears.

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CLINICAL DIFFERENTIAL DEMONSTRATION OF UTERINE AND TUBAL CONTRACTIONS BY KYMOGRAPHIC UTEROTUBAL INSUFFLATION*

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FROM the beginning of uterotubal insufflation as a clinical nonoperative test for tubal patency, it was noticed that during insufflation, pressure oscillations were manifest on the mercury manometer in most cases and absent in others. The oscillations were always present when the Fallopian tubes were found to be freely patent. In nonpatent tubes, pressure oscillations were invariably absent.

Guthmann[1] was one of the first to observe and attempt to explain this difference in manometric fluctuations. However, it was some time before its full significance was realized. In 1925 adopting a kymograph to the insufflation apparatus, I began a more detailed study of this question, the results of which were published in November, 1927.[2]

In the work just referred to, it was demonstrated that the kymographic tracings observed during uterotubal insufflation are due to rhythmic contractions and relaxations of the tubal muscle; also that these pressure fluctuations are absent when the tubes are closed; and last, that the uterus is passive in the vast majority of cases during the insufflation, its contractility being inhibited by distention.

Two circumstances have led to renewed interest in this question. First, the statement by Knaus,[3] and others, that the uterus undergoes changes in motility which vary with the interval of the ovulation-menstrual cycle; and, second, the recurring doubt by some as to the true nature of the

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oscillations noted during uterotubal insufflation which they believe to be manifestations of uterine muscle activity and not of the tubes.

In 1937 and 1938 two of my associates undertook to clarify this question by experimental work on the uterus and oviducts of live rabbits. The work of S. Wimpfheimer and M. Feresten[4, 5] is of sufficient interest to be summarized briefly:

Procedure

Using 60 mature female rabbits weighing from 2 to 4 kilograms, they demonstrated that when a leak is made into the uterus, preventing the CO_2 gas from passing through the oviducts, the pressure oscillations become profoundly altered; that the isthmus and intramural portion of the oviducts influence the manometric fluctuations whether the insufflation proceeds through the uterus or through the tubes; no contractions take place when the oviducts have been cut away and the uterine segment alone is present and widely open. Furthermore, if the uterus is completely sidetracked by inserting the cannula directly into the uterotubal junction, the kymographic tracings continue practically unaltered.

The direct effect upon uterine and tubal motions was still further checked in the living rabbit by fastening fine hooks to segments of the uterine muscle and tubal muscle previous to insufflation and during insufflation. The action of the tubal and uterine muscle thus transmitted was recorded on a lampblack-coated paper on one kymograph while the dynamic changes taking place through insufflation were simultaneously recorded on another kymograph. This demonstrated that while the action of the tubal muscle was uninfluenced during insufflation there was a marked change in the action of the uterine muscle which exhibited shallow contractions in three instances and disappeared almost altogether in two instances. It should be pointed out that the tubes become partially distended by the CO_2 gas which has the possibility of escaping through the abdominal ends. The uterus, however, is more or less constantly under the same degree of distention contingent upon the resistance of the narrow apertures of the uterotubal junctions above and the mechanical obturation below. This last experiment would seem to be quite conclusive; nevertheless the question continues to be raised from time to time.

Among those who have questioned the above conclusions is Stabile,[6] of Montevideo, who in a recent paper presents a painstaking inquiry into the nature of the oscillations observed during kymographic uterotubal insufflation. He feels apparently that the oscillations thus produced are due to changes in uterine and muscle tonicity which undergoes certain variations due to regurgitation of the CO_2 gas from the tube as a sort of "garrulitas tubae." His conclusions are based upon observations he made upon living tubes and uterus at laparotomy. These observations have raised points which may well serve as the basis for discussion of the whole question of tubal vs. uterine contractions. Owing to the limited time and space allotted for this paper I shall not enter into all the moot questions.

Stabile believes that "because distention of the tube takes place coincident with the rise in pressure and the tubal souffle heard by auscultation coincides with the drop in pressure, therefore tubal contractions

are ruled out relegating to the tubes a passive role." As this, in my opinion, is a basic contradiction it may be well to describe the action of the CO_2 gas and the reaction of the uterus and tubes to the CO_2 as it streams through the genital tract in the normal case. When CO_2 is insufflated into the uterus under airtight conditions at the cervix the uterus distends until such point where the narrow apertures of the uterine ostiae of the tubes are passed and at which point the gas must make its way through the tube lumen.

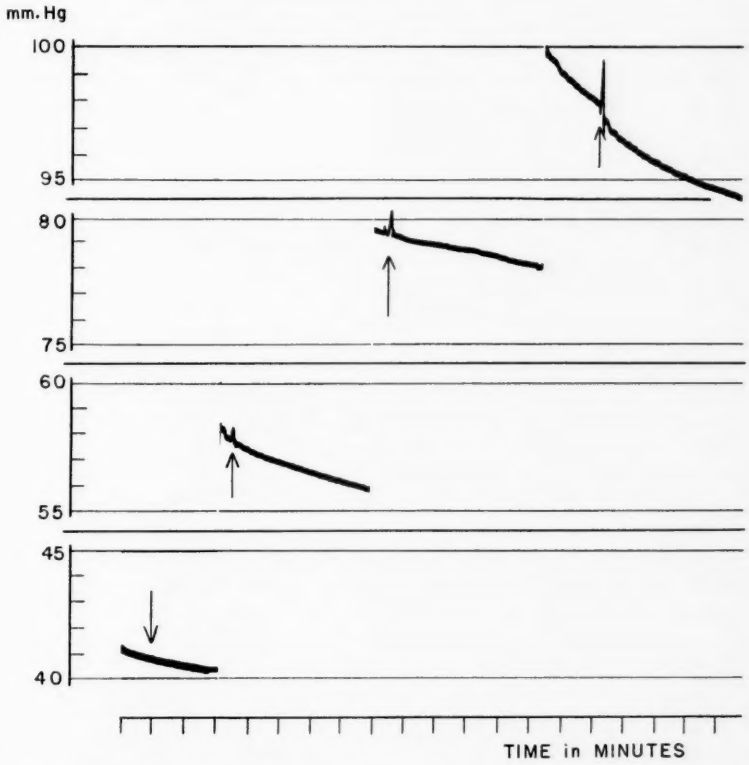

Fig. 1.—Showing degree of distention of the uterine cavity necessary for voluntary straining of the patient's abdominal muscles or manual compression of the abdominal wall to produce pressure effects on the uterus. In this case no pressure effects are visible at 41 mm. Hg while increasing effects are demonstrable at 58, 79, and 98 mm. Hg. The pressure necessary in this case to convert the virtual uterine cavity into a distended cavity is between 41 and 58 mm. Hg.

The pressure begins to rise the moment gas is forced into the uterus. As the uterine cavity is only virtual in the nonpregnant normal state, the uterine walls approximating each other and kept in apposition by the tonicity of the uterine muscle, a certain pressure is required to convert it into an actual cavity through distention. This varies according to my observations between 40 and 60 mm. Hg in the average case (Fig. 1). The pressure rises during the distention until such point when the uterine openings of the tubes are passed. The amount of pressure necessary to accomplish this depends upon the tonicity of the

uterotubal junction, the muscle sphincter of the intramural portion of the tube and its actual diameter.

In the course of its passage through uterus and Fallopian tubes the CO_2 gas meets with five resistances. The first has already been mentioned within the uterus; the second is the intramural portion; the third are the approximated walls of the tubes which are held in apposition by a certain tonicity of the tubal muscle; fourth, a sort of sphincter action at the isthmicoampullary junction and, fifth, a less developed sphincter at the fimbriated end.

Once the fimbriated end has been passed, the pressure drops. It must be borne in mind that the pressure mechanism of the apparatus insures a constant rate of flow of the insufflated gas. During the state of contraction, the tube becomes distended gradually and progressively from the uterine to the fimbriated end by the continuous insufflation of the CO_2 under a constant rate of flow until the fimbriated end is reached when the gas can escape into the peritoneal cavity. This we take to coincide with the moment of relaxation. Then contraction begins anew and the same mechanical process is repeated in a rhythmic fashion. If no contractions, followed by relaxations, took place, there should be no rhythmic oscillations of the manometer. That is to say if the CO_2 gas had only to overcome muscular tonicity it is conceivable that there would be an initial rise of pressure which should be enough to equalize and then exceed the dynamic resistance of the muscle. But once this was overcome there would be no other factor to prevent the continuous uninterrupted flow of gas through the tubes as the insufflating force is vastly greater than that encountered in the tube lumen. However, if one assumes that the tubes undergo rhythmic contractions, a fact borne out by visual observations on the intact organs and by numerous experiments on tubal muscle strips (Seckinger and Snyder,[7] Corner,[8] R. T. Frank[9]) then the oscillations observed on the kymograph during uterotubal insufflation in normal tubal patency are clearly accounted for.

Observations

The tubes contract as a whole and segmentally. If the tube of a rabbit is cut into segments from the fimbriated end toward the uterine end during uterotubal insufflation, it will be found that the isthmus and the intramural portion exhibit the most marked contractions while the force of the latter is relatively less in the ampullary portion and very weak in the fimbrial portion. If the sections are reversed in fimbrial (tubouterine) insufflation, practically the same results are obtainable. The same effects have been demonstrated in the surviving human Fallopian tubes.

In interpreting the graphs obtained by uterotubal insufflation, one must take cognizance of the fact that the CO_2 gas is introduced at a constant rate of flow and if the tubes had no inherent motility the CO_2 gas would be forced through them at a uniformly steady rate. There would be no pressure oscillations, the gas escaping at a constant flow rate of bubbles through the fimbriated ends and not intermittently as actually observed. When the tubal muscle undergoes contraction, the gas flow is momentarily intercepted by the tightening and narrowing of the tube lumen. This causes a rise of pressure. The moment the muscle relaxes the lumen is widened and the gas escapes with a drop

of pressure. The kymograph records both the pressure rise and fall. The CO_2 gas streaming through the Fallopian tubes acts as an elastic medium upon which muscle activity is recorded and in many instances, small, almost inaudible bubbles may be observed during the rise of pressure which is due to the fact that the tube lumen is not completely obliterated. The escaping bubbles under this circumstance are not squeezed out by the tubal contractions but by the driving force of the insufflating apparatus.

The number of oscillations is to a certain degree dependent upon the volume of gas transmitted through the tubes at a given rate. A certain amount of irritation due to increased pressure and possibly as a result of the CO_2 itself accompanies the rapid rate flow while very slow rates diminish the contraction relaxation rate. For this reason we have recommended a constant flow rate of 60 c.c. per minute for purposes of comparison in studying the effects of hormonal tubal contractility.[10, 11]

The graphs obtained in clinical uterotubal insufflation either represent synchronous activity of both tubes or of the one tube which permits the CO_2 to pass through it at a lower pressure than it takes to pass through the other tube. I have frequently demonstrated this on the surviving and nonsurviving extirpated organs and also clinically as well as upon the manikin. The lumina of the tubes are not invariably equal and the tonicity also varies not infrequently, a fact recorded also by Whitelaw,[12] Randall,[13] and Mocquot and Palmer.[14] Spastic muscle contractions may be produced by the galvanic current applied to the tube muscle, and if CO_2 is passing through the tube lumen a rise of pressure will be noted coincident with the blanching and constriction of the muscle. A similar effect was produced in the *Macacus rhesus* by pituitrin which by its oxytocic action either abolished the tubal contractions altogether for a few minutes or reduced their amplitude and frequency (A. H. Morse and I. C. Rubin[11]).

Another clinical proof of the fact that rhythmic contractions as observed during uterotubal insufflation are due to the action of the tubal muscle is their complete absence or serious modification when the Fallopian tubes are adherent or strictured. The pathologic condition has been corroborated by many laparotomy observations. That no oscillations occur when both tubes are completely obstructed has already been mentioned. In this circumstance the tubes are paralyzed by the overdistention produced by the CO_2 gas proximal to the obstruction. If the obstruction is located at the uterine ends, the uterus becomes overdistended and fails to exhibit rhythmic contractions. If the tubes are adherent but incompletely obstructed, allowing the CO_2 to pass through the narrowed lumen, the rhythm is altered. The graph produced shows a higher initial pressure with a gradual sloping downward as the CO_2 passes through the constricted point. Depending upon the degree of stricture rhythmic fluctuations are either absent altogether or if present they are as a rule shallow and irregular, indicating the extent to which the tubal muscle has become pathologically altered and functionally impaired.

The clinical incidence of this tubal status with incomplete stenosis (stricture or adhesions) is considerable accounting for from 15 to 25 per cent of all sterility cases.

A clinical experimental demonstration of the fact that the pressure oscillations observed during uterotubal insufflation are conditioned by the action of the tubal muscle has been afforded in instances where temporary sterilization is accomplished by immobilizing the Fallopian

tubes underneath the vesicouterine peritoneum. In this operation the fimbriated ends of the tubes are dislocated into the vesicouterine space where the edges of the tubes are sewn together at several points and fastened to the connective tissue as well as the uterine wall. If the tubes are insufflated a week or two after the operation the graph obtained will show complete absence of contractions although these were demonstrable before the tubes were transfixed. The CO_2 passes into the subperitoneal space where it produces the crepitus characteristic of gas collection. By means of uterosalpingography with any crystalloid iodine solution the transfixed dislocated Fallopian tubes may be visualized as well as the spill into the subperitoneal space of the vesicouterine fossa.

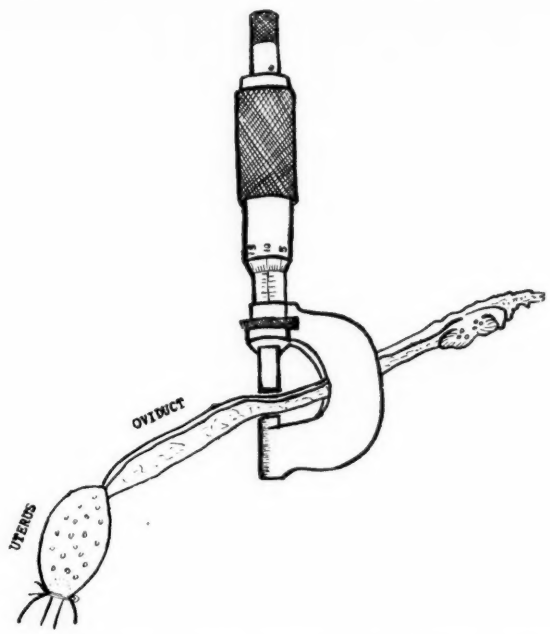

Fig. 2.—Micrometer clamp applied to the rabbit's oviduct.

In surviving extirpated uterus and tubes, it is possible to reproduce the contraction-relaxation phenomenon as observed during clinical insufflation. By immobilizing or constricting such Fallopian tubes, one can note the effect on the pattern of contractions. If the tubes (or one tube, the other being clamped off) are pinned down to a cork mat, the pins being inserted through the seromuscular edge thus preventing free motion, it will be seen that the rhythmic contractions disappear. If the pins are removed, the rhythmic contractions reappear, showing the passive part played by the uterus during the insufflation.

Artificial strictures of living and surviving tubes may be reproduced by applying clamps at any point of their course. This was accomplished in a number of living rabbits by means of a micrometric clamp gauged by notches to measure a thousandth of an inch (Figs. 2 and 3). It was used primarily to help in the calculation of the degree of stricture met clinically and determined by kymographic uterine insufflation. By

means of such a clamp one gets an idea of the changes in the kymographic tracing produced by pathologic strictures encountered clinically. These vary from mild flattening out of the rhythmic oscillations to their complete disappearance. The results are similar in the living and surviving organs. Removal of the clamp is followed by restoration of the tubal motility.

As I have had occasion to observe previously, nonfunctioning Fallopian tubes as encountered in prolonged amenorrhea, fail to exhibit rhythmic contractions altogether or manifest occasional motions more or less weak. The low level of pressure, indicating poor muscle tone which is always present in such instances, distinguishes this condition from tubal strictures which are marked by high elevations of pressure.

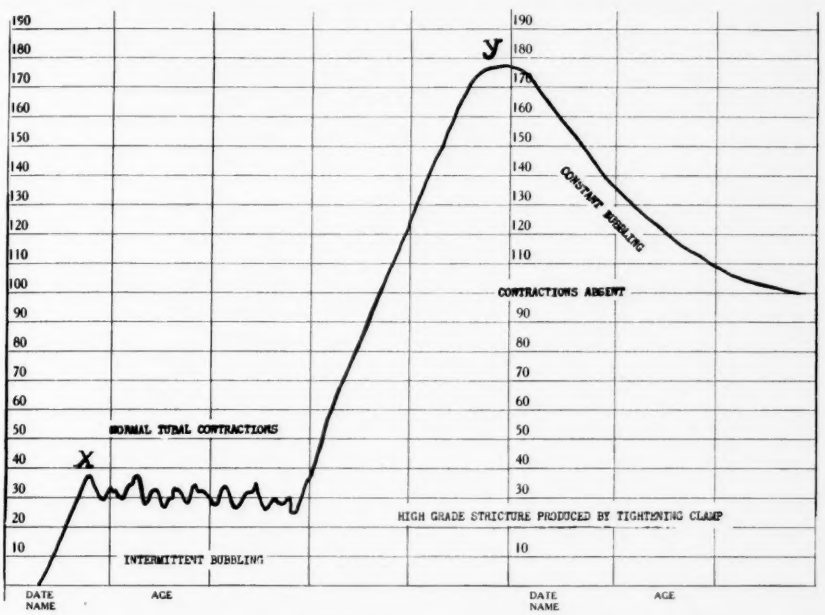

Fig. 3.—Showing the effect of constriction (stenosis) upon tubal contractility. Note pressure increase from 38 mm. Hg at *X* to 178 mm. Hg at *Y* after constriction and resultant abolition of contractions.

In 1927,[2] I stated that the rhythmic waves recorded on the kymograph during uterotubal insufflation are "not due to uterine contractions which in the nonpregnant state have so far not been demonstrated." Since then the literature abounds in reports upon uterine motility in the pregnant and nonpregnant state. The excellent work of C. Moir,[15] S. R. M. Reynolds,[16] of F. Falls,[17] of F. L. Adair,[18] and their collaborators is well known. Although my chief attention was focused upon tubal contractions, the possibility of demonstrating uterine motility by transuterine insufflation has been constantly in mind. The first step in this direction was the realization that the insufflation apparatus was not sensitive enough to record uterine changes. The water siphon meter contains an air chamber which dampens the registration of uterine motility. The air chamber of the siphon meter has a capacity much greater in proportion to the few cubic centimeters compressed within

the uterine cavity. The pressure waves are therefore much reduced, practically neutralized in the siphon meter. This does not influence the pressure effects produced by the action of the tubal muscle because the amplitude of the latter is considerably greater than that of the uterus. Hence my departure in using aneroid manometers and other systems which have been of decided help in accomplishing results.

Although my conclusions regarding tubal contractility have been accepted by most workers, as for example Rucker,[19] Mocquot, Palmer, Lejeune and Raizi,[20] Geist, Salmon and Mintz,[21] Bernstein and Feresten,[22] and S. Wimpfheimer,[4, 5] who based their work on the original hypothesis, I have considered it worth while to reopen the question of tubal versus uterine contractions adding further clinical observations which have recently been made.

We have endeavored during the last two years to study uterine contractility apart from tubal contractility in women under different clinical circumstances: early stages of pregnancy including hydatid mole, dysmenorrhea, metrorrhagia with and without fimbromyomas and in normal cases. The study has been facilitated by improvement in apparatus which has enabled us to carry out observations previously not possible.

As far as the tubes are concerned the rhythmic oscillations recorded on the kymograph during uterotubal insufflation by means of the siphon meter are actually in the main similar to those which are obtained when an aneroid manometer and photoelectric recorder are used. For small variations in pressure, the two last mentioned are more sensitive.

We have overcome the disadvantage of the siphon meter in studying uterine contractions by adopting an aneroid system with CO_2 as the medium in one apparatus (Grafax) and another using a fine pin valve (Foregger) in which the air chamber is reduced practically to zero. A third method utilizes a sensitive photoelectrical recorder with a water manometer which brings out the uterine action more graphically (Feitelberg).

These three systems have enabled us to demonstrate satisfactory motions of the uterus.* The media used were CO_2, saline solution, viscous ray opaque and hippuran injected into the free uterine cavity; and CO_2, air or saline within an intrauterine balloon.

To obtain graphs of the action of the uterine muscle the CO_2 is subjected to a pressure below that required for the gas to pass through the tubes. This is readily predetermined by testing the pressure necessary for the gas to pass through the uterotubal junction. If for example the initial pressure rise is 80 mm. Hg a pressure of not more than 50 or 60 mm. Hg will be maintained. The CO_2 within the uterine cavity serves the same purpose as air in an intrauterine balloon.

It will be noted from the tracings recorded when CO_2 gas is confined within the uterine cavity or is (encased) in the balloon or when salt solution is used (Figs. 4, 5, 6) that the type of contractions is similer in each case but that they differ materially from the pattern produced when CO_2 gas passes through the tubes. We have found that the uterus manifests contractility when distended by different media provided the

*The data obtained from the use of the newer apparatus will be presented in a separate paper by Drs. S. Feitelberg, A. Davids and myself.

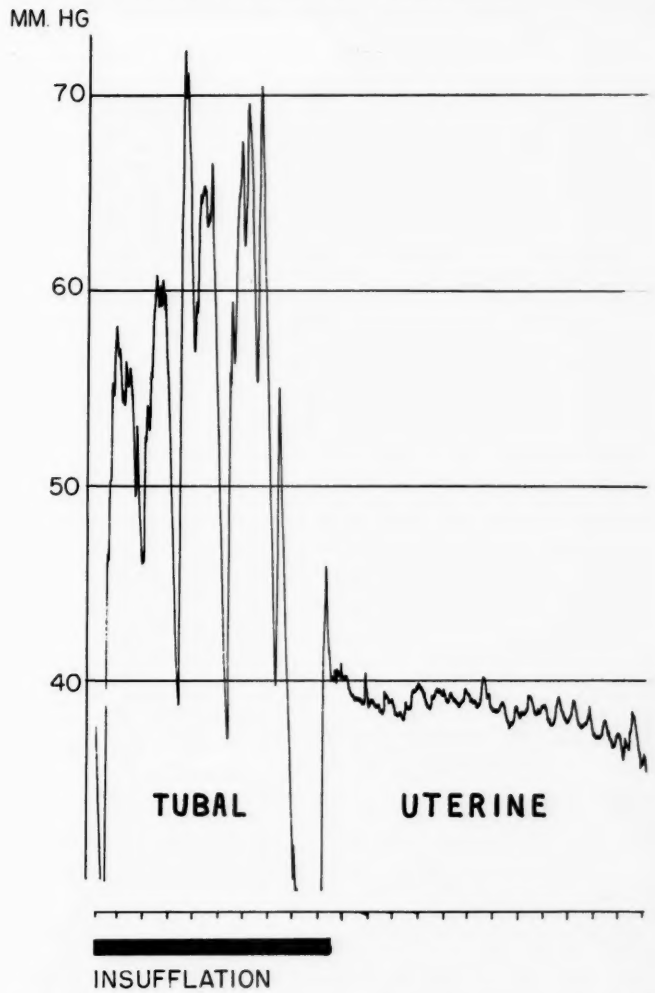

Fig. 4.—Note that the amplitude of uterine contractions varies between ⅓ mm. Hg and 2 mm. Hg (Grafax insufflation apparatus) whereas the amplitude of tubal contractions ranges between 10 mm. Hg and 20 mm. Hg (photoelectric recorder).

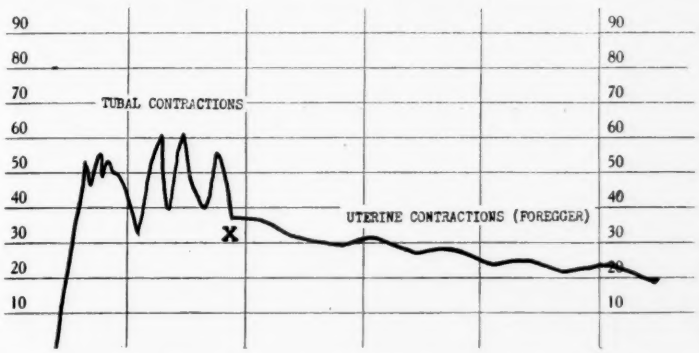

Fig. 5.—The contrast is just as striking between the tubal and uterine contractions when the CO_2 gas flow is stopped, *X*, and the uterine cavity contains CO_2 only at a pressure of 35 mm. Hg. (Foregger apparatus.)

degree of distention is not excessive. As there are 13 mm. of water to 1 mm. Hg the oscillations are magnified 13 times the size of the graph obtained by the mercurial manometer. The ink writer in the photoelectric recorder is controlled by a motor, hence the lag due to friction on the drum is much less than that produced by a floater. Whether uterine contractions are recorded by this apparatus or by an aneroid system, their force has been found in the nonpregnant state to average between ⅓ and ½ mm. Hg to 1½ mm. Hg as compared to a range of 30:40 mm. Hg exhibited by the tubes. They are also less frequent per minute.

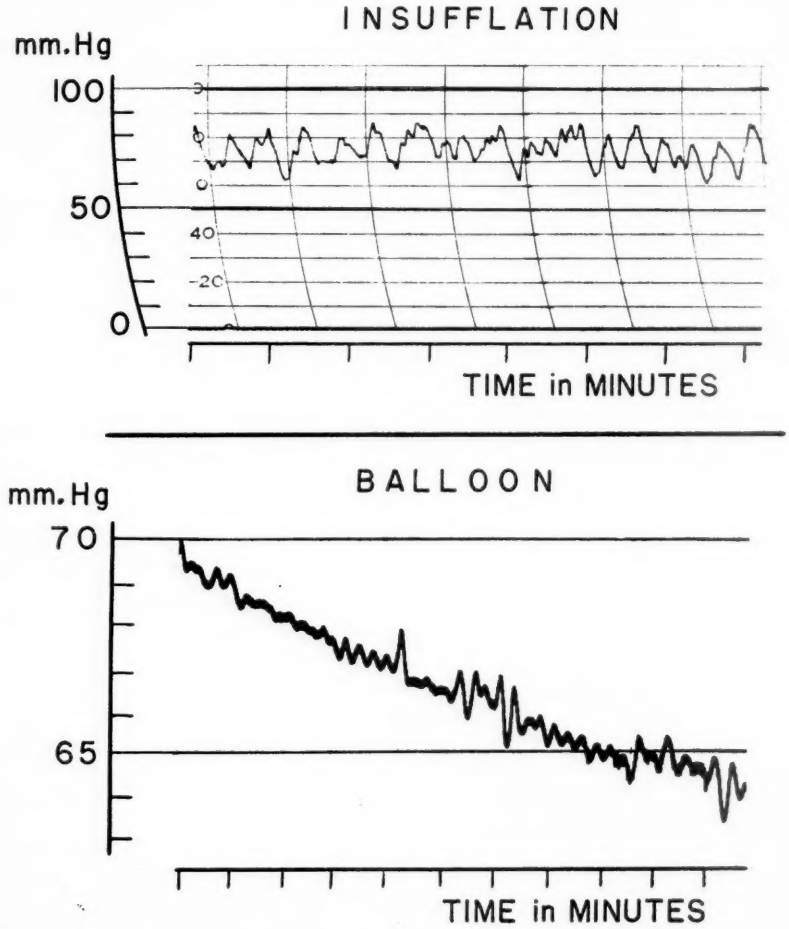

Fig. 6.—Showing contrast between amplitude of oscillations produced by tubal contractions recorded by an aneroid manometer (Grafax) and the very shallow oscillations produced by uterine contractions recorded by means of an intrauterine balloon. (Photoelectric recorder.)

When solutions are used, the intrauterine pressure is carefully noted avoiding pressures which would force the fluid through the tubes. This is readily determined previously by insufflating with CO_2 in order to note the level at which the CO_2 gas passes from the uterus into and through the tubes. However, as a further check the pelvic organs were exposed to x-rays and films were taken at various points of the injection.

Hippuran was used for this purpose and appeared to have no appreciable influence over the character of the uterine contractions as previously elicited by sterile saline solution. The solution was injected in a uniform pressure rate flow by the force of CO_2 gas from the insufflating apparatus (Fig. 7). X-ray visualization of the tubes was thus made possible at a rate comparable to the flow of CO_2 gas which gave the opportunity to observe whether and to what extent tubal motions were demonstrable by their effect upon the column of fluid. These motions are extremely superficial when a viscous contrast medium is used.

Although uterine contractions may be thus best studied in cases where both tubes had been removed comparing the results with balloon experiments and the results obtained in cases having intact Fallopian tubes, it was considered desirable to compare the results in the same case where tubal contractions could be elicited apart from uterine contractions. This was carried out in a number of instances.

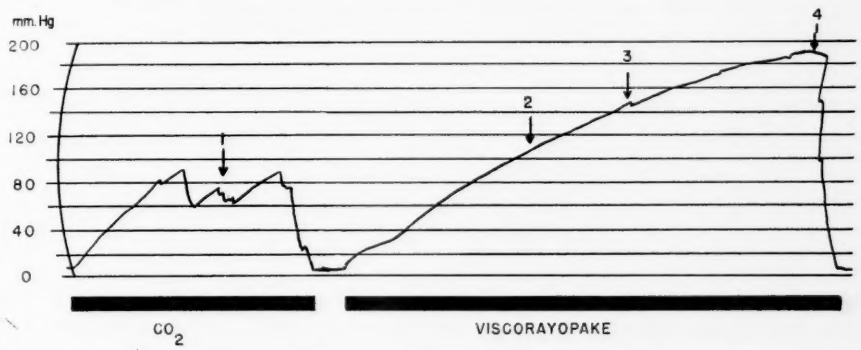

Fig. 7.—Kymographic tracing of uterotubal insufflation with CO_2 contrasted to that obtained by injection of a viscous ray opaque contrast medium at the same rate flow.

In a most recent experiment, the uterus and tubes were insufflated in the usual way. The graph thus obtained served for comparison. Following this procedure the parametria were injected with 1 per cent novocain solution. It could not be predicted to what degree the character of the contractions would be changed nor whether the uterus was completely paralyzed and with it possibly the tubes. The method of injection obviously includes the possibility of affecting the innervation of the tubes as well as of that of the uterus. That uterine or tubal motions are not dependent entirely upon nervous influences has been demonstrated upon the surviving extirpated organs. However, the infiltration was intended to produce a mechanical barrier which should in any event inhibit the motion of the myometrium.

Although the novocain infiltration could not be exclusively limited to the myometrium and parametrium leaving the mesosalpinx free, the result of this one experiment demonstrated that despite complete loss of motion in the uterine muscle the tubes may retain more or less the same power of contractions as they exhibited during uterotubal insufflation before the parametria were infiltrated with the novocain solution.

Mocquot has insisted for a long time and his hysterographic observations with lipiodol under manometric control using low pressures appear to corroborate his contention that: the great majority of pathologic uteri have either a much diminished contractility or none. In their

10 cases, contractility was absent in four (one cancer; two metropathias; one hypoplasia with sterility); weak in four (two metrorrhagia of probably ovarian origin; one hypoplasia with amenorrhea; one uterus subnormal probably due to hypofolliculinization); strong in two cases (one fibroma; one abortion). Even in the cases where the contraction has been marked, it was not produced before a pressure of 4 cm. of mercury.

The number of cases upon which Mocquot has based his conclusions and of my own cases in this respect is not large enough for statistical purposes. As far as it goes the same general law applies to pathologic uteri as for pathologic Fallopian tubes, namely that their contractility is either lost altogether or becomes more or less reduced.

Summary

Recent clinical observations and experimental work on living and surviving genital organs of the rabbit by means of kymographic uterotubal insufflation have confirmed earlier conclusions.

The kymograph tracings of manometric oscillations observed during uterotubal insufflation represent rhythmic tubal contractions and relaxations. They are not due to changes in tonicity per se but to actual contractions whose rate varies per minute in accordance most probably with the particular phase of the ovulation menstruation cycle. The nonpregnant uterus has been demonstrated to exhibit a contraction relaxation phenomenon under suitable distention and recorded by appropriate manometric devices. The character of the contractions differs in each organ, the uterus in general undergoing slower motions of much shallower force. The pressure medium in the uterus may be solutions, gas or air without balloon enclosure and with an intrauterine balloon. The ideal pressure medium within the lumen of the tubes has been found to be CO_2 gas which is insufflated at a constant rate of flow. Salt solution or other fluid injected through the tubes under a constant pressure rate flow has been found unsuited in comparison with CO_2 in the present setup for the recording of pressure oscillations emanating from the tubes. Adoption of aneroid manometers and a photoelectric recorder has helped in establishing the difference in pattern between tubal and uterine contractions in the same and different cases.

I wish to express my appreciation for cooperation in this study to Dr. S. Feitelberg, physicist to Mt. Sinai Hospital, and Dr. Arthur M. Davids; and also to Mrs. Carl Pforzheimer, Jr., who rendered valuable technical assistance.

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Discussion

DR. M. PIERCE RUCKER, Richmond, Va.—The question Dr. Rubin proposes is not whether the nonpregnant uterus contracts or whether the tubes contract, but what causes the waves encountered during an insufflation of normal tubes. What the pen on the manometer records is the pressure of the CO_2. If the gas is flowing at a constant pressure, the wavelike variations in the record can be caused only by variations in the outflow. The most logical place to look for this variation in the outflow is in the narrowest part of the system, i.e., the tubes. The situation is very much like a millpond with a constant stream feeding the pond. To vary the "head" of water you put more or less obstruction in the mill race. The same amount of obstruction in the pond itself would have no effect whatever.

It seems to me that Dr. Rubin had already proved conclusively that the waves are due to tubal contractions. He now proves that they are due to the contraction of the narrowest part of the tube. The fact that you get no waves when the tubes are closed would indicate that the contractions of the uterus have nothing to do with it. He has also shown with extirpated organs that the fall in pressure coincides with relaxation of the tubes, and a rise with the contraction of the tubes.

One point only touched upon is that the contraction of neither uterus nor tubes is powerful enough to be shown working against a pressure of from 60 to 110 mm. of Hg or to be recorded when there is so much compressible gas in the tubing. When Knauss' work first came out I tried to repeat it with an ordinary Rubin apparatus but failed completely. In fact, the only time I have been able to record contractions of a nonpregnant uterus was when the recording system was entirely filled with water.

The fact that diseased tubes may be patent but show no waves of contraction and relaxation is an important clinical observation. When such tubes are found in the course of a sterility study, treatment with foreign protein injections, or with heat, will frequently restore them to a normal condition and the waves will appear in the kymographic record.

I note that Dr. Rubin is investigating contractions of the nonpregnant uterus, and I look forward to seeing this phase of his work appear more in detail.

DR. RUBIN (closing).—Those shallow uterine contractions that we see in the nonpregnant state range between a millimeter and a millimeter and one-half of mercury, and are tremendously intensified in the pregnant state. We have had occasion to observe this wide range in fluctuations with the photoelectric recorder in cases of second and third months of pregnancy in a number of instances before inducing a therapeutic abortion.

HYDATIDIFORM MOLE AND ASSOCIATED TUMORS OF THE CHORION*

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(From the Department of Obstetrics and Gynecology, University of Virginia)

THE introduction of the biologic tests for gonadotropic substances in the urine, which are strongly positive in instances of abnormal chorionic activity, has stimulated a renewed interest in disturbances of the chorion. The literature in recent years contains numerous articles dealing with various phases of the subject, some of which present an optimism which hardly seems justified in view of the past experiences with this bizarre group of disorders. The most common of the diseases of the chorion is hydatidiform mole. Whether hydatidiform mole is primarily a neoplastic or a degenerative process still seems unsettled. Virchow believed that the process was essentially a myxomatous degeneration of the connective tissue of the chorionic villi, and designated it as myxoma chorii. Recently Hertig[1] after a rather extensive study also suggests that the degenerative process is primary and that the epithelial proliferation is secondary to the degenerative changes. In 1895 Marchand[2] pointed out that the essential feature was an irregular and profuse proliferation of the chorionic epithelium, and it still seems to be generally accepted that the proliferative changes are the primary lesions.

The diagnosis of a hydatidiform mole in the uterus before the passage of some of the vesicles is often difficult, but occasionally can be accomplished. The most significant symptom in our experience has been a slight but persistent dark bloody discharge from the uterus. In one instance the diagnosis was made in a patient with such a history, who was presumed to have a threatened abortion, but who developed, while under observation, bilateral cystic ovaries. In another case the diagnosis was made in an instance of presumed pregnancy, from the history of slight persistent vaginal bleeding and the presence of ovarian cystomas. The absence of fetal outlines by x-ray examination in those cases in which the uterus is as large as or larger than a sixteen weeks' pregnancy, practically establishes the diagnosis. Disproportion between the size of the uterus and the duration of the presumed pregnancy is a helpful sign when present, but this discrepancy is not always present, and in a few of our cases the uterus was actually smaller than was anticipated for the duration of the pregnancy. The presence of large amounts of gonado-

*Presented, by invitation, at the Fifty-Fifth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons at Hot Springs, Virginia, September 10 to 12, 1942.

tropic substances in the urine in cases of mole has led to attempts to establish the diagnosis by quantitative determinations while recently gonadotropins have been found in the spinal fluid in cases of hydatidiform mole.

The majority of hydatidiform moles are either spontaneously passed or may be removed through the vagina. Some cases, particularly those in the older age group in whom the diagnosis is established before the passage of vesicles, may be more satisfactorily managed by hysterectomy. The manner of removing the mole requires an individualization of each patient. An important part in the treatment is the subsequent examinations of the patient including tests for urinary gonadotropin.

Many instances of hydatidiform mole are definitely benign, and following their passage no serious sequelae develop, while others show a marked tendency to proliferation and to invasion of the uterine and pelvic blood vessels, often with metastatic nodules in the uterine and vaginal walls, so that the mole is considered as malignant or destructive. For this group Ewing[3] proposed the term chorioadenoma destruens. Others imply that there is but little justification for this term, and prefer to consider the malignant type of mole simply as a milder variant of chorionepithelioma. Our attempts to distinguish between a benign and malignant mole by examination of the vesicular material which is passed, have been fruitless, and we are unable to predict from the gross and microscopic examination of the vesicular material which of the moles have already invaded the pelvic tissues or which ones will subsequently be followed by invasive chorionic cells. However, some believe that the malignant types show either an invasion of the stroma of the villi with epithelial elements, anaplasia of the epithelium, or chorioepithelial elements growing detached from the villous structures. After removal of the uterus, we have classified some of our cases as malignant moles or chorioadenomas because of marked proliferation of Langhans' cells and syncytium, and local extension, but with preservation of villous outlines. Two of these seem of sufficient interest to justify a brief synopsis of their records.

Case 1.—(No. 60215.) Mrs. P., a 49-year-old white woman, who had had three previous pregnancies, had the last normal menstrual period in August. Some vaginal bleeding began in October and continued until her admission to the hospital in December. Examination showed, in addition to an enlarged softened uterus, a firm nontender mass the size of a walnut on the anterior vaginal wall just to the left of the urethra. On a presumptive diagnosis of hydatidiform mole, a hysterectomy and a bilateral salpingo-oophorectomy were performed. A microscopic diagnosis of chorioadenoma was made because of the rather extensive invasion of the uterine wall by syncytium and Langhans' cells. On the second postoperative day vaginal bleeding occurred, and an examination showed it to be arising from the nodule in the vagina, which had apparently eroded through the mucosal surface. Tissue from the nodule revealed chorionic villi and proliferating Langhans' cells. The cystic

area was excised. A Friedman test was still strongly positive one month after operation. A course of x-ray therapy was given over the pelvis, and two weeks later the Friedman test was negative. The Friedman test has remained negative, and the patient has now survived for nine years.

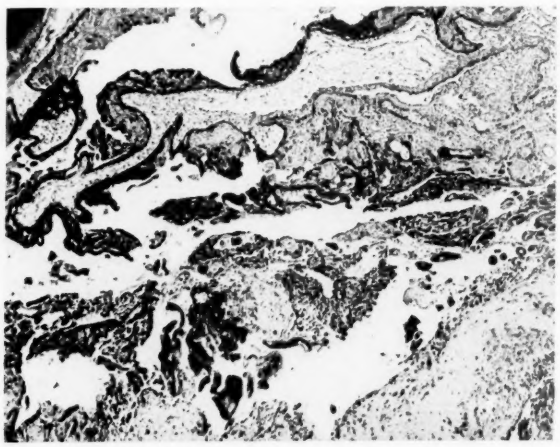

Fig. 1.—Mrs. P. (Case 60215). Chorionic villus, Langhans' cells, and syncytium in uterine wall. ×50.

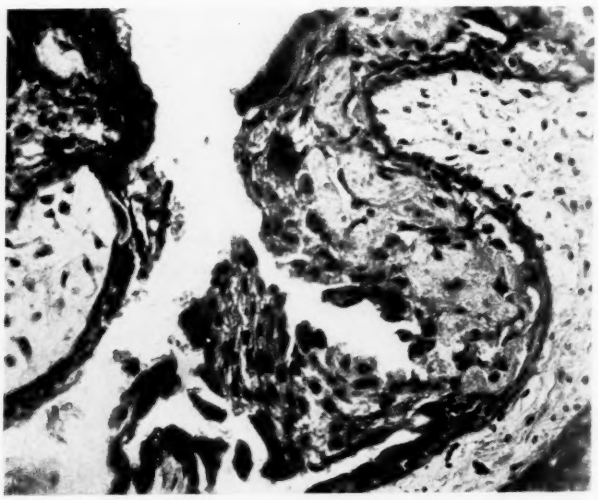

Fig. 2.—Mrs. P. (Case 60215). High power of an area in Fig. 1, showing villus and Langhans' cells and syncytium. ×240.

CASE 2.—(No. 130279.) Mrs. J. H. K., a 24-year-old white woman, had her last menstrual period Nov. 7, 1936. A slight bloody discharge had been present since December, while moderate bleeding had been present since March 5, 1937. She was admitted to the hospital on March 15, when examination showed the uterus to be the size of a four months' pregnancy, with a cystic mass palpable to the right of the uterus. An x-ray picture showed no evidence of a fetal skeleton. With a tentative

diagnosis of hydatidiform mole and a lutein cystoma of the right ovary, a bougie was inserted in the uterus, and a mole evacuated twelve hours later. Two months later the Friedman was strongly positive, although the right ovary seemed to be decreasing in size. A curettage was done,

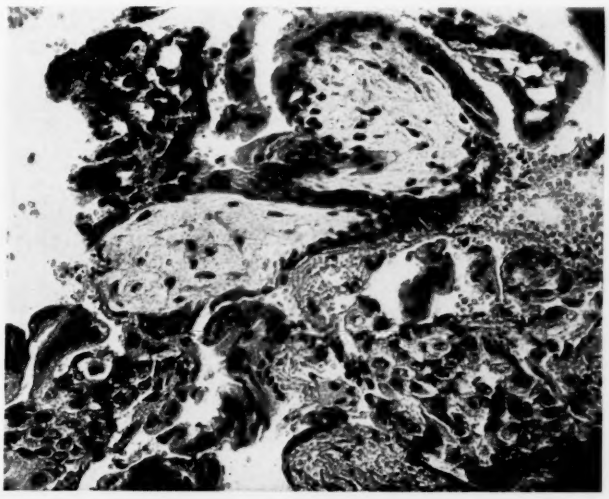

Fig. 3.—Mrs. P. (Case 60215). Section from vaginal nodule. Chorionic villi, Langhans' cells, and syncytium. ×57.

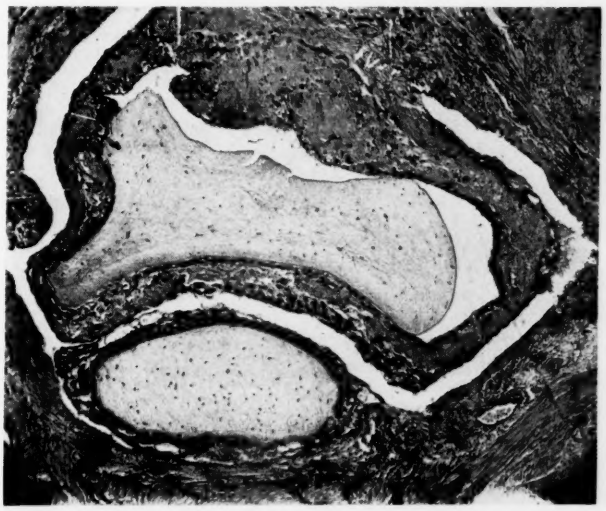

Fig. 4.—Mrs. J. H. K. (Case 130279). Section from uterine wall showing vein containing chorionic villi and Langhans' cells. ×55.

the tissue revealing only an endometritis with a decidual reaction. One month later, three months after the passage of the mole, the Friedman was still strongly positive, so that on a presumptive diagnosis of chorion-epithelioma, a hysterectomy and a bilateral salpingo-oophorectomy were done. At the time of operation masses of mucoid material were present in the right broad ligament, and the right uterine vein was distended

and filled with mucoid material. Pathologic examination showed villous structures and chorionic cells invading the veins of the uterus. Lutein cysts were present in both ovaries. One month later the Friedman test was still strongly positive, and 8,000 r. of x-ray therapy were given over the pelvis through four portals. X-ray pictures of the chest were negative and the pelvis and vagina were free. Six months after operation and five months after radiation the Friedman test was negative for the first time. Four months later, ten months after operation, in spite of normal chest and pelvis, the Friedman became positive again, and remained positive for ten months. One year later (January, 1940) the test became negative and has remained negative and the patient remains well.

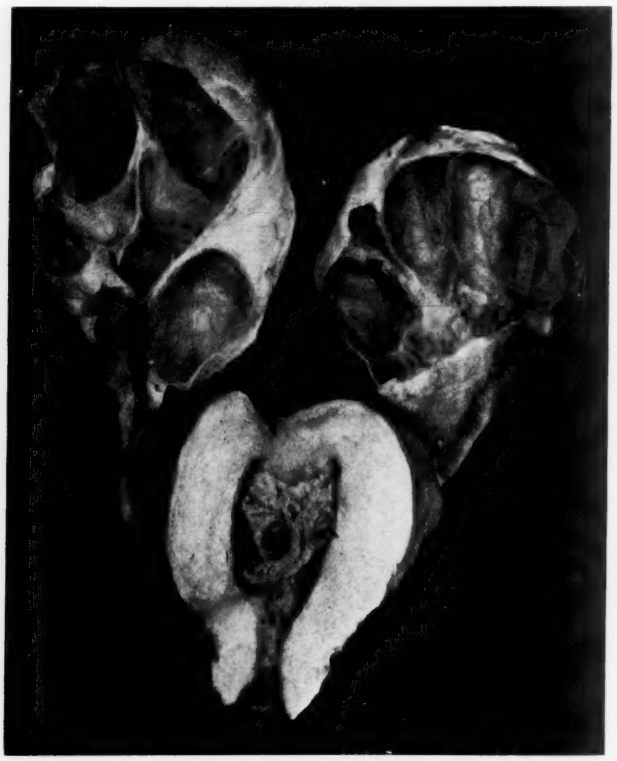

Fig. 5.—Mrs. D. J. T. (Case 110100). Gross specimen showing mass of tissue on posterior uterine wall. Bilateral lutein cysts.

A syncytial infiltration of the uterine wall with an associated inflammatory reaction may occur, a condition commonly spoken of as syncytial endometritis, although originally described as an atypical chorionepithelioma. Its designation as a tumor is open to question, although at times the uterus is enlarged and infiltrated by a bulky mass with neoplastic characteristics, in which case it is spoken of as syncytioma. In these conditions it is assumed that no Langhans' cells are present but only syncytium. The following case is one of this nature.

Case 3.—(No. 110100.) Mrs. D. J. T., a 19-year-old white woman, who in 1934 had eclampsia, was admitted in October, 1938, with the uterus

the size of a five months' pregnancy with hypertension, albuminuria, and edema. Eight days after admission, a mole was spontaneously passed from the uterus with profuse hemorrhage requiring massive transfusions. After passage of the mole, a large cyst was found filling the pelvis. One month later (December, 1938) the Friedman was negative, although orange-sized bilateral ovarian cysts were present. One month later (January, 1939) the Friedman was positive again, some abnormal uterine bleeding was present, the uterus was enlarged to about twice the normal size, and the cysts seemed larger than at the time of the previous examination. An x-ray of the chest was normal. Hysterectomy and bilateral salpingo-oophorectomy were done. The pathologic diagnosis was syncytioma and lutein cysts. Two weeks later the Friedman was negative, has remained negative, and the patient remains well.

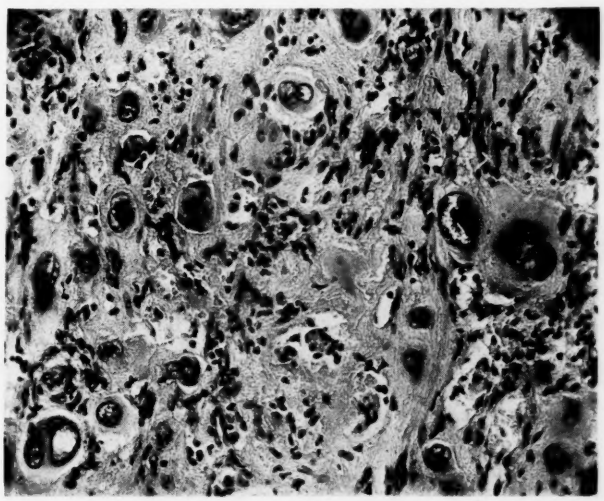

Fig. 6.—Mrs. D. J. T. (Case 110100). Section through mass in posterior uterine wall showing syncytial cells. ×57.

We reserve the term chorionepithelioma for the highly malignant tumor, consisting of a disorderly growth of both Langhans' cells and syncytium with an absence of villous formation. The growing masses of tumor cells splits the uterine muscle with destruction of tissue, necrosis, and hemorrhage, invades the sinuses, and is characterized by widespread metastases, particularly to the lungs and brain. We feel that this is a highly fatal tumor, and the four cases of this type in our records have all died. Fortunately this very malignant type seems to be rare. Of the four cases in our series three followed the passage of moles, while one was a primary chorionepithelioma of the Fallopian tube, which has been previously reported.[4]

We have had in following patients, with Friedman tests, after pregnancies or moles, two cases of passing interest.

Case 4.—(No. 121613.) Mrs. E. T., a 36-year-old white woman, was delivered at full term on Nov. 3, 1935, since which time there had been

some vaginal bleeding until admission to the hospital on Feb. 12, 1936. During the three months prior to admission two curettages were done by her local physician to control the bleeding. Examination revealed an apparently normal sized uterus with a similar-sized mass to the right which was thought to be an ovarian cyst. A Friedman test was strongly positive. A preliminary curettage was attempted, but the uterine sound met no obstruction beyond the cervix, so that a diagnosis of instrumental perforation of the uterus was made. On exploration through an abdominal incision, a bicornuate uterus with an old perforation between the two horns and a small submucous fibromyoma in one horn was found. Hysterectomy and bilateral salpingo-oophorectomy were done. A rather careful gross and microscopic examination of the structures removed failed to reveal any chorionic tissues, and no lutein cysts were found in the ovaries, the only one of our cases in which they were not found on microscopical examination. Three weeks following operation, the Friedman was still positive, but was negative in six weeks, has remained negative since, and the patient remains well.

TABLE I. PATIENTS WITH HYDATIDIFORM MOLE AND ASSOCIATED TUMORS

CASE	AGE	CONDITION	REMARKS	RESULT
1	19	Mole	Vaginal delivery, followed for only 7 months	Well?
2	27	Mole	Vaginal delivery	Well
3	27	Mole	Vaginal delivery	Well
4	45	Mole	Vaginal delivery	Well
5	18	Mole	Vaginal delivery	Well
6	19	Mole	Vaginal delivery	Well
7	21	Mole	Toxemia, vaginal delivery	Well
8	20	Mole	Vaginal delivery, pregnancy 2 years later with eclampsia	Well
9	15	Mole	Vaginal delivery, normal pregnancy 1 year later	Well
10	20	Mole	Vaginal delivery, normal pregnancy 2 years later	Well
11	30	Mole	Vaginal delivery, normal pregnancy 4 years later	Well
12	22	Mole	Vaginal delivery, D. and C., syncytial endometritis	Well
13	30	Mole	Vaginal delivery, positive Friedman 3 mo. later; D. and C. Normal pregnancy removed, uneventful pregnancy 2 years later	Well
14	51	Mole	Hysterectomy	Well
15	26	Mole	Hysterectomy	Well
16	26	Mole	Hysterectomy, twisted lutein cyst	Well
17	49	Mole	Vaginal metastases (excision), hysterectomy, radiation	Well
18	19	Mole	Toxemia, vaginal delivery, syncytioma, hysterectomy	Well
19	34	Mole	Vaginal delivery, syncytioma, hysterectomy	Well
20	43	Mole	Vaginal delivery, syncytioma, hysterectomy	Well
21	24	Mole	Vaginal delivery, chorioadenoma, hysterectomy	Well
22	26	Mole	Chorionepithelioma of broad ligament 1 year later. Inoperable, radiation, pulmonary metastases	Death
23	35	Mole	Chorionepithelioma 3 mo. later, hysterectomy, 1 month later brain metastases	Death
24	19	Mole	Exploration and biopsy 6 mo. later. Inoperable chorionepithelioma. Death assumed	Death
25	23	Primary chorionepithelioma of tube, hysterectomy, radiation, brain metastasis		Death
26	36	Positive Friedman and bleeding after normal pregnancy. D. & C., perforated double uterus, hysterectomy, no chorionic tissue		Well

In another patient, who had passed a mole in June 1939, the Friedman was still positive and the uterus slightly enlarged three months later. A

curettage was performed and a normal pregnancy removed from the uterus. The patient has since passed through a normal pregnancy and an uneventful delivery.

We have records of 24 patients who passed moles, and in addition one patient with a primary chorionepithelioma of the Fallopian tube, and one case of a persistent positive Friedman with uterine bleeding for three months after a normal pregnancy. Of the 24 patients with moles, 4 had them removed by hysterectomy and 20 passed them through the vagina. Thirteen of the 20 whose moles were delivered through the vagina had an uneventful recovery, although one of the patients in a subsequent pregnancy had a spontaneous rupture of the uterus, probably from a weak spot in the uterine wall as a result of invasion of the wall with chorionic tissue. Curettage in this patient two weeks after passage of the mole produced a large quantity of tissue, which was diagnosed as syncytial endometritis. Four of the 20, who were delivered through the vagina, had positive Friedman's tests following the moles and were treated by hysterectomy, one diagnosed as chorioadenoma and three as syncytioma. All of these patients have survived. The other three who passed the moles through the vagina developed chorionepithelioma, all of them occurring before the use of the biologic tests in the subsequent examination and observation of patients who have passed moles. The patients who had a diagnosis of chorionepithelioma died.

TABLE II. ANALYSIS OF CASES

	NUMBER
Moles passed through vagina, uneventful recovery	13
Moles delivered by hysterectomy, uneventful recovery	4
Moles passed, positive Friedman, hysterectomy	
Chorioadenoma	1
Syncytioma	3
Moles passed, subsequent chorionepithelioma	3
Primary chorionepithelioma of tube	1
Positive Friedman and bleeding 3 mo. following normal pregnancy and delivery. No chorionic tissue found	1
Total	26

TABLE III. HYDATIDIFORM MOLES

	NUMBER	PER CENT
Delivered by hysterectomy	4	16.7
Vaginal delivery, uneventful recovery	13	54.2
Vaginal delivery followed by chorioadenoma	1	4.1
Vaginal delivery followed by syncytioma	3	12.5
Vaginal delivery followed by chorionepithelioma	3	12.5
Total	24	100.0

Discussion

One of the most interesting developments in the consideration of chorionic growths is the use of the biologic tests for urinary gonadotropic substances in the diagnosis and prognosis. These hormones are often

present in excessive amounts in the urine and apparently also in the spinal fluid in instances of chorionic growths. The presence of a positive test indicates the presence of viable chorionic tissues, but the frequency with which the test becomes negative and then subsequently positive, indicates that too much reliance should not be placed on a single negative test. The presence of a persistent positive test following a mole, abortion, or pregnancy justifies the diagnosis of persistent viable chorionic cells, although in one of our cases with bleeding and a positive test three months post partum, no chorionic tissue was identified in the uterus, tubes, or ovaries. It is quite likely that a small nest of cells was overlooked, although many sections were taken. In another instance, another pregnancy had supervened within three months of the passage of a mole, and although its possibility was considered, we were reluctant to rely upon it. While curettage is often helpful and is commonly used in the follow-up of these patients, negative findings may be entirely misleading, and the procedure is not without danger. Obviously the curette will not obtain tissue from masses outside of the uterine cavity, which is a rather common situation.

The problem, which always presents itself, is what course to pursue in the presence of a persistent positive test following the passage of a mole, an abortion, or term pregnancy. While we are justified in assuming the presence of chorionic tissue, are we justified in radical operative procedures on the assumption that a chorionepithelioma is present? We have perhaps erred on the radical side, but the hope of removing or preventing a chorionepithelioma has possibly justified our course. This course has in our hands resulted in radical procedures for chorioadenomas and syncytiomas, the termination of a normal pregnancy, and in one case the inability to find any chorionic tissues in the removed structures. It is our custom in the presence of a persistent positive test to perform a curettage, and if a month or so later the test is still positive, we believe that an abdominal exploration of the pelvis with hysterectomy is advisable.

The question arises whether apparently benign chorionic tissues remaining in the uterine walls and the vessels of the uterus and pelvis may not subsequently assume malignant characteristics. The same consideration arises in regard to deported chorionic tissue (deportation of chorionic villi). Apparently the question cannot be answered with certainty, but one is inclined to believe that they may. This would explain the presence of metastatic lesions with an absence of any primary malignant lesion in the uterus. One of our cases of chorionepithelioma manifested itself as a hemorrhagic mass in the right broad ligament one year after an early abortion with vesicular villi. At abdominal exploration the uterus was small and separate from the mass. The mass in the right broad ligament was inoperable and was treated by radiation. The patient, however, died of pulmonary metastases shortly after the radia-

tion. Occurrences of this nature suggest that chorionic tissue remaining either inside or outside of the uterus may eventually assume malignant qualities. If this contention is correct then probably a radical method of treatment is justified in those cases in which chorionic tissue remains in the pelvis, invading uterine walls and vessels, whether we call them benign or malignant moles, chorioadenomas, syncytiomas, or milder variants of chorionepitheliomas.

The presence at times of lutein cysts in the ovaries in association with chorionic growths has long been recognized, and their general tendency to retrogress following the passage of a hydatidiform mole is well known. Their frequency as reported in the literature seems to be dependent upon them being of sufficient size to permit detection on physical examination. In some cases, however, they are not sufficiently large to be definitely palpated on bimanual examination. They have been found microscopically in all of our cases in which the ovaries were removed and in which chorionic tissues were present in the pelvis, although in some the ovaries were not sufficiently enlarged to detect them on vaginal and abdominal examination. In two of our cases the cysts had partially twisted on their pedicles and gave rise to sufficient symptoms to require their removal.

Our experience, with these chorionic tissues which persist in the pelvis after the passage of a mole, suggests that the prognosis varies with the presence or absence of villous structures and with the presence or absence of proliferating Langhans' cells. All patients in our cases which we have classified as benign hydatidiform mole, malignant mole or chorioadenoma, and syncytioma have survived, while those in cases classified as chorionepithelioma, masses of Langhans' cells and syncytium without villi, have died. If this is generally true it might seem to justify an attempt to classify them on some such basis as that proposed by Ewing.[3]

Summary

A discussion of hydatidiform moles and their subsequent course with a review of 24 cases is presented. The mole may be benign, its passage complete and recovery may be uneventful. In others, approximately one-half of our cases, chorionic tissues remain in the uterine cavity or in the uterine walls, and cause persistent positive biologic pregnancy tests.

We have classified these cases microscopically as syncytial endometritis or syncytioma (infiltration with syncytium only), malignant mole or chorioadenoma (syncytium, Langhans' cells and villi), or chorionepithelioma (Langhans' cells and syncytium).

Those diagnosed on this basis as chorionepithelioma have died, while all of the others have survived.

I wish to express my appreciation to Dr. James R. Cash and to the other members of the Department of Pathology, for the pathologic studies and for invaluable aid and suggestions in the preparation of this material. I am indebted to Dr. J. R. Cash of the Department of Pathology and to Dr. J. R. Kight of the Department of Obstetrics and Gynecology for the preparation of the photomicrographs.

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Discussion

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD.—After a patient has been delivered of an hydatidiform mole, what is the best means of detecting, at the earliest possible moment, the development of chorionepithelioma? Since the histologic picture presented by hydatidiform mole is often unreliable as a prognostic guide and since clinical phenomena may be misleading, Dr. Williams rightly emphasizes the importance of endocrine observations in following these patients. But, as he points out, here also pitfalls await us. Occasionally, the test may become negative, turn positive again, and later show once more a negative reaction. We have observed this in one of our cases, as have others. Moreover, Schumann has reported a case in which a chorionepithelioma developed six months after a supposed miscarriage although repeated hormonal tests in the interim had been negative. Others have reported bizarre and irreconcilable results of a similar character.

But even if it be granted that hormonal tests have been misleading in occasional instances of this disorder, it must also be admitted that in most cases they follow a definite pattern and are of great value. It would seem desirable, therefore, to look carefully into this question and ask if there is any way in which endocrine studies can be made to serve our purpose more reliably than they have at times in the past. That serum gonadotropin does follow a definite pattern following the expulsion of an hydatidiform mole *in the average case* is shown by the studies of Brindeau, Hinglais, and Hinglais. Basing their statements on 86 cases, they found that their patients fell into three main groups. In Group I, the serum gonadotropin fell rapidly to zero within two or three weeks; in Group II, it disappeared slowly, the mean time of disappearance in this group being almost eight weeks; there was great variability, however, and in 3 cases small amounts of gonadotropin were still present in the serum after three months; in Group III, the serum gonadotropin decreased for a few weeks and then showed a sudden upturn. The moles in Group I and II were all benign, as shown by the subsequent clinical course, while the patients in Group III developed chorionepithelioma. The authors, therefore, lay great stress on the secondary upward swing of gonadotropin, but this can only be demonstrated, of course, by quantitative assay.

Dr. Eleanor Delfs of our Clinic has had the opportunity of following one case of hydatidiform mole with quantitative serum gonadotropin assays with results which are shown in Table I. At the time of expulsion of the mole, the concentration

TABLE I. SERUM GONADOTROPIN* FOLLOWING DELIVERY OF HYDATID MOLE

Case E. McK.—188903

Day	½	11	20	29	36	43	50	64	78	106
Units/L	515,000	12,000	11,600	2,600	570	350	225	0	0	0

*International standard units of chorionic gonadotropin.

of the hormone in the serum was very high, a half-million units per liter, but this fell rapidly to reach 2,600 units by the twenty-ninth day. This patient still showed serum hormone levels between 200 and 500 units between the thirty-sixth and fiftieth day, and it should be pointed out particularly that these lower levels might or might not have given a positive Friedman reaction, depending upon the concentration of the urine, the condition of the rabbit, etc. In other words, it is conceivable that we

might have obtained a negative Friedman reaction on the thirty-sixth day, a positive one on the forty-third day, and again a negative response on the fiftieth day, despite the fact that the serum hormone concentration was decreasing in a smooth and normal manner. Only quantitative assays can give clear-cut evidence of this progressive decrease. Likewise, in the series of Brindeau, Hinglais, and Hinglais, a small fraction of their cases continued to show small amounts of hormone in the serum for three to five months, borderline amounts which might or might not have given a positive Friedman, depending on the circumstances mentioned above.

It would thus appear that the Friedman test, although of the utmost value in the diagnosis of pregnancy, is not sufficiently delicate to reveal accurately the progressive decrease in gonadotropin which follows the expulsion of benign moles. Accordingly, the gist of my discussion is to suggest the employment of quantitative assays on the serum in following patients after hydatidiform mole. Laborious as these assays are, the gravity of chorionepithelioma is such as to justify the trouble. By this means it seems possible that some of the bizarre and irreconcilable results heretofore reported may be avoided.

DR. EMIL NOVAK, BALTIMORE, MD.—The confusion in the nomenclature of the diseases described by Dr. Williams pertains not only to terms but also to interpretations. The intermediate type of lesion, to which the name chorioadenoma destruens was applied by Ewing, is not a clearly defined group. The term itself has always seemed to me a badly selected one, being based on a supposed similarity of the chorionic villi with gland structures, when as a matter of fact they much more strongly suggest, histologically and functionally, the villi of the intestine.

There is rarely any difficulty in the histologic diagnosis of a frankly benign mole or of a frank chorionepithelioma. But there is an intermediate group of cases in which pathologists will differ, chiefly because of differences in criteria as to histologic malignancy. Such attributes as penetration of blood vessels, to which some attach great importance, would seem unreliable in view of the fact that the villi and trophoblast of normal pregnancy penetrate vascular channels, while similar penetration is often seen in hydatidiform moles which by their clinical course are obviously benign. Nor is trophoblastic overgrowth in itself a safe criterion, as clinically benign moles may show extensive trophoblastic proliferation. This is especially true of villi still attached to the uterine wall, while the degenerated villi usually constituting the grapelike masses filling the uterine cavity may show little or no proliferation.

In the chorionepithelioma on which all pathologists will agree, there is not only a lawless overgrowth of the trophoblast in columns or islands which invade and destroy the musculature, as indicated by extensive coagulation necrosis, but there is usually a loss of the villous pattern. There are exceptions to this, but when this villous pattern is well preserved, I have been inclined to lean backward in the diagnosis of malignancy.

It would seem that the sensible plan is to recognize gradations of malignancy with these lesions as with other forms of malignancy. If the so-called chorioadenoma destruens, or the "malignant mole" of other writers, is really clinically malignant, why not consider it a chorionepithelioma of a lesser degree of malignancy than the very frank chorionepithelioma which I have just discussed? By the same token the term adenoma malignum, used by so many pathologists, is better spoken of as adenocarcinoma of Grade I.

As for the biologic tests, valuable as they are, they may lead us astray, as Dr. Williams has emphasized, so that we are now evaluating them more circumspectly than we formerly did. If the quantitative test remains strongly positive for many weeks or months after the evacuation of a mole, most gynecologists will feel justified in performing hysterectomy, and their attitude cannot be criticized in view of the grave possibilities to the patient. But I am convinced that in a very large propor-

tion of such cases chorionepithelioma will not be found. Instead of this, one will often discover that the chorionic hormone production has been kept up by incompletely removed but benign hydatidiform mole. In many cases the molar tissue is actually irremovable by curettage, because it may have penetrated deeply into the maternal vascular channels. This was true, for example, in one of the patients included in Dr. Williams' series whom I had the opportunity, through his kindness, of observing with him, and I have had similar experiences with a number of other patients.

DR. FOSTER S. KELLOGG, BOSTON, MASS.—Is there any validity in the theory that an immediate study of the mole material will give an indication as to whether that mole will become malignant? Our pathologist at the Boston Lying-in Hospital is of the opinion from his work that, at least in a certain number of instances, he is able from the frozen sections to say that the mole is potentially malignant and that hysterectomy at that time is justified on this basis.

DR. GEORGE M. SHIPTON, PITTSFIELD, MASS.—We have had the disappointing experience of being mistaken on the Friedman test in the diagnosis of an ordinary pregnancy. Of course, it is generally accepted that there is a 5 per cent error and for that reason many people do two rabbit tests instead of making a single test. I would like to ask just how many rabbits were used in the tests which he refers to as negatives that should not have existed as negatives?

DR. WILLIAMS (closing).—Dr. Eastman's suggestion in regard to quantitative serum determinations seems to be of real value. With the facilities available to us, however, we have been unable to make these determinations.

In answer to Dr. Kellogg's question regarding the diagnosis by examination of the vesicular material passed, all I can say is that we have been unable to determine whether or not it has malignant potentialities or whether masses of chorionic tissue remain in the vessels and walls of the uterus.

Dr. Shipton raised the question of the number of tests which were made. While we have simply stated that a Friedman was negative or positive, these have been on the basis of repeated tests. Several are usually done before any radical procedure is considered in a young woman.

SARCOMA OF THE UTERUS*

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TRUE primary sarcomas of the uterus are recognized clinically as highly malignant tumors. Unfortunately the histologic diagnosis of sarcoma in the uterus is often difficult when the neoplastic picture appears in association with myomas. Patient and doctor alike are fortunate in that sarcomas associated with grossly appreciable fibroids often do not prove clinically malignant. So-called secondary sarcomas, these relatively benign tumors, apparently arise by sarcomatous transformation in degenerating myomas.

Our observations regarding sarcoma of the uterus have been largely directed to the problem of diagnosis in the doubtful or borderline case. The records of our patients have been studied in an effort to recognize when cellular irregularities in rapidly growing or degenerating myomas become sarcomas capable of initiating a clinically malignant course. In 57 instances we know the patient's length of survival, date of death, or present physical condition. However, few autopsies have been obtained and in most instances we lack proof that patients died of sarcoma. For the most part, conclusions have been based on the number of patients known to be living at the present time.

Incidence

The records of the Buffalo General Hospital during the past 21 years list the diagnosis of sarcoma of the uterus in 46 cases. Comparing these 46 sarcomas with 3,686 fibroids and 577 carcinomas of the uterus treated during this interval, we found an incidence of one sarcoma in 80 fibroids and one sarcoma in every 12.5 malignancies of the uterus. These figures indicate a surprisingly high incidence of sarcoma compared with Searight's[1] report of 3,203 fibroids and 576 carcinomas of the uterus with only 12 sarcomas during the same period of time. However, Goldberger[2] noted one sarcoma in 100 fibroids, and Smith,[3] in 1941, reporting from Memorial Hospital, where a high incidence of malignant tumors would be expected, found one sarcoma in each 47 fibroids examined. Novak and Anderson[4] have reported that 3.1 per cent of the uterine malignancies sectioned in their laboratory were sarcomas. At the University of Pennsylvania, Kimbrough[5] found an incidence of 3.2 per cent. Searight's report agrees with the frequently quoted figure of one sarcoma to every 40 carcinomas of the uterus. This same frequency was noted by Scudder and Fein[6] in 1934; by Handley and Howkins[7] in 1937, and Kotz and Kaufman[8] in 1938.

*Presented, by invitation, at the Fifty-Fifth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 10 to 12, 1942.

The general incidence of sarcoma of the uterus is doubtlessly somewhat lower than the average of figures quoted in reports of individual observers. This viewpoint seems verified by statistics made available by Dr. Louis C. Kress,[9] Director of the Division of Cancer Control of the Department of Health of the State of New York. During the year 1941, as successful operation of the cancer reporting law became a reality in New York State, a total of 1,661 malignancies of the uterus were reported. Thirty-four cases, 2.04 per cent, were reported to be sarcomas, an incidence of one sarcoma for each 48.8 carcinomas of the uterus.

Variation in the reported frequency of sarcoma of the uterus may in part be accounted for by differences in the criteria upon which observers have based their diagnosis. Our own material included 7 cases that should not be considered in a study of sarcoma of the uterus (Table I).

TABLE I. INCIDENCE OF SARCOMA OF THE UTERUS

In the Buffalo General Hospital
1920-1941 Inclusive

DIAGNOSIS OF TUMOR		NUMBER OF CASES	
Fibromyoma of uterus			3686
Carcinoma of the uterus (cervix and fundus)		577	
"Sarcoma of the uterus"		46	
Cases reclassified and omitted			
Uterine sarcoma proved secondary at autopsy	1		
Carcinosarcomas	3		
Atypical myomas reclassified nonmalignant	3		
Total	7		
Sarcomas associated with myomas	12		
Sarcomas in uteri showing no fibroids	27		
Total cases considered as sarcomas	39		
Incidence of sarcoma			
As a malignant tumor of uterus (1 to 15.6 carcinomas)		6.33%	
In patients operated for myomas (1 to 96 fibroids)			1.04%
Associated with degenerating myomas		1 per 307 fibroids	

In one instance at autopsy a previously recorded sarcoma of the uterus was proved to be secondary to primary sarcoma of the adrenal gland. In 3 cases the clinician had recorded a diagnosis of sarcoma on patients in whom the pathologist had noted only atypical cellularity in fibroids. Three other cases of so-called carcinosarcoma had been listed as sarcomas of the uterus. Excluding these 7 cases, the remaining 39 represent an incidence of one sarcoma in every 15.6 malignancies of the uterus, and one sarcoma in each 96 fibroids treated during the years 1920 to 1941.

Malignant Degeneration in Fibroids

Varied interpretation of controversial slides accounts for a wide discrepancy in the reported incidence of sarcomatous change in myomas. Figures as high as 10 per cent have been reported but there is general agreement that not more than 1 per cent of myomas undergo malignant change. Novak and Anderson[4] reported that 0.56 per cent of their fibroids should be so classified, a figure supported by Kimbrough,[5] who noted an incidence of 0.76 per cent in his material. Reviewing the histologic reports of 1,400 of our fibroids, in 12 we noted atypical changes that might be interpreted as early sarcomatous transformation. This

represents one fibroid showing areas of atypical cellularity in each 116 myomas examined, an incidence of 0.85 per cent. It is interesting to consider this figure in view of the fact that among sarcomas found in our Hospital, while 12 were associated with myomas, only 7 were considered examples of sarcomatous transformation in degenerating myomas. Our incidence of malignant degeneration in fibroids is therefore only 0.19 per cent, one sarcoma in each 526 fibroids.

Classification

Classifications of sarcomas of the uterus generally prove unsatisfactory because, as Novak[10] has concisely stated, "the invasive tendency of sarcoma soon tends to blot out the evidences of its origin." In relatively early cases grouping can be based on the suspected tissue of origin, but in the majority of reports sarcomas of the uterus have been classified according to the dominant type of neoplastic cell (Table II). Grouping

TABLE II. PROGNOSIS IN SARCOMA OF THE UTERUS

Classified According to Histology of Tumor

HISTOLOGIC GROUPING	TOTAL CASES	CASES LIVING	LENGTH OF TIME SURVIVORS FOLLOWED	DECEASED	LENGTH OF SURVIVAL
Sarcomatous degeneration in fibroids	7	7	2—3 years 4—5 years 1—6 years	0	—
Giant cell sarcoma	2	0	—	2	1— 2 mo. 1—10 mo.
Mixed cell sarcoma	3	0	—	3	1—op. 1— 2 mo. 1— 6 mo.
Round cell sarcoma	4	0	—	4	2— 2 mo. 1— 6 mo. 1—36 mo.
Spindle cell sarcoma	10	2	1—12 years 1—14 years	8	1—? 1—op. 1— 1 mo. 1— 2 mo. 3— 6 mo. 1—16 mo.
Endometrial sarcoma	10	3	1—2½ years 1—5 years 1—14 years	7	2— 2 mo. 1— 3 mo. 1— 9 mo. 2—12 mo. 1—22 mo.
Totals	36	12	—	24	—

Of 29 cases operated prior to 1938, 9 (31%) have survived 5 or more years.

Of 8 sarcomas associated with fibroids operated prior to 1938, 6 (75%) have survived 5+ years.

Of 21 sarcomas in uteri not containing fibroids operated prior to 1938, only 3 (14.3%) have survived 5+ years.

our cases in this manner, when the cell type is correlated with the patient's clinical course, there is noticeable variation in the degree of clinical malignancy manifest by different types of sarcoma. Three of the 39 sarcomas listed in Table I have been excluded from this grouping.

While follow-up data were obtained on 2 of the 3 omitted cases, slides are no longer available and the histologic diagnosis was recorded simply as sarcoma of the uterus. Seven of the 12 tumors arising in uteri containing myomas were considered by the pathologist as originating by sarcomatous degeneration in fibroids. Two of these patients have been followed for over three years, the remaining 5 for over five years, but none of this group have shown any evidence of metastasis or the recurrence of a pelvic tumor. Compared with the rapidly fatal course noted in patients with a giant, mixed or round cell type of tumor, this table shows an occasional long time survival by patients whose tumors were designated as spindle cell sarcoma. Likewise, in the group considered to be primarily of endometrial origin, 3 patients have survived for two and one-half, five, and fourteen years.

One patient surviving fourteen years is of particular interest. Grossly and histologically a typical case of sarcoma botyroides, an 8-year-old girl was treated by Dr. James E. King in 1928, by local excision of the tumor from the cervix followed by two small-dose applications of radium in the cervical canal. Now 22 years old, the patient is having fairly regular periods and on examination the uterus and adnexa appear to be normal. We have noted no other reports in the literature of long term survival of a patient treated for this usually highly malignant form of sarcoma.

Considering the 39 cases listed in Table I, we found that 29, operated prior to 1938, could be utilized in calculating a five-year survival rate. Follow-up information was obtained on all 29 patients in this group. Nine were found to be free of symptoms after five years, a cure rate of 31 per cent. Six of 8 patients operated prior to 1938, in which a sarcoma was found associated with fibroids, have survived over five years. This figure for curability is in striking contrast to the results noted when patients were found to have sarcomas unassociated with myomas of the uterus. In this group only 3 of 21 patients survived five years, a five-year survival rate of 14.3 per cent in primary uterine sarcomas.

Symptomatology

The diagnosis of sarcoma of the uterus is rarely made before operation. The symptoms and findings usually suggest a preoperative diagnosis of fibromyoma of the uterus. Observers agree that irregular vaginal bleeding is the most frequent complaint. Watery discharge is often noted by patients with an endometrial type of sarcoma. A rate of growth more rapid than ordinarily noted in benign tumors should warrant a suspicion of the malignant character of the neoplasm. The case recently reported by Anderson and Lomax[11] emphasizes the malignant potentialities of rapidly recurring polyps. Abnormally rapid growth should always be regarded with suspicion in spite of a reassuringly negative histology. Pain has been frequently noted as a comparatively early symptom in sarcoma as compared to the late occurrence

of pain in carcinoma of the uterus. To make the diagnosis when malignancy of the uterus is removable we must remain apprehensive concerning irregular or post-menopausal bleeding. Hopeless malignancy will develop if we readily conclude that abnormal bleeding is due to a palpable, but possible incidental fibroid.

Treatment

Effective treatment of sarcoma of the uterus depends upon wide surgical removal of all pelvic tissue that can be sacrificed. The predisposition of these tumors to postoperative thrombo-embolism should be remembered. Care should be taken to avoid injuring venous channels proximal to the point of ligation. After a subtotal hysterectomy for supposedly benign fibroids, when sarcoma is reported, the operator is confronted with the problem of possible malignancy in the remaining cervix. Dannreuther[12] and others have expressed the opinion that a secondary operation for removal of the cervix subjects the patient to greater danger than the probability of extension from the cervix. A study of our material substantiates the wisdom of a conservative course, although in at least one instance we could ascribe recurrence of pelvic sarcoma to extension from a cervical stump. In a majority of cases it seems probable that sarcoma arising in the fundus and involving the cervix at the time of operation would have extended beyond removable limits, in which case secondary removal of the retained cervical stump could add nothing to the five-year salvage among these patients. Several observers have reminded us that radium can be satisfactorily applied postoperatively in the cervical stump, a measure involving far less risk to the patient than a secondary operation for removal of the cervix.

According to Masson,[13] the 1920 German Gynecological Council concluded that results following irradiation therapy were so good that no operation was advised when this diagnosis was proved or suspected. In his own material Masson noted that irradiation was of no appreciable value in at least one-fourth of the cases treated at the Mayo Clinic. Our observations suggest that palliative benefit can be realized by irradiation of the more anaplastic types of uterine sarcoma. The relatively long survival of several patients in Groups C and D treated by radium and x-ray therapy is shown in Table III. The effectiveness of irradiation is most apparent in patients treated preoperatively by intrauterine applications of radium for suspected carcinoma of the uterus. Healy[14] and others have expressed pessimism regarding the results of irradiation in sarcoma of the uterus. However, on the basis of comparatively limited observations, we believe it would be advisable to employ intrauterine radium before panhysterectomy in the treatment of the highly cellular sarcomas of endometrial origin. On the other hand, we have found that postoperative roentgen therapy appears to accomplish very little, particularly in cases of the histologically more mature types of myogenic sarcoma.

Discussion

Credit for the first attempt to correlate the histologic picture with the patient's clinical course should go to Proper and Simpson,[15] who in 1919 noted large atypical nuclei and giant cells occurring in direct proportion to the clinical degree of malignancy. In doubtful cases these observers suggested the absence of mitotic figures as a dependable criterion of benign growth. Their interpretation of the significance of mitotic figures has been repeatedly verified by later studies. Difficulties in interpretation of the histology of these uterine sarcomas were evident in 1920, when Evans,[16] quoted Kelly and Cullen as stating that while they found 17 sarcomas of the uterus among 1,400 myomas removed, during the same period of time they had noted 17 other tumors in which the diagnosis of sarcoma was questionable. Combining a correlation of the histology and the clinical course of the patient, Evans reported an evaluation of 9 histologic characteristics previously described by various observers as reliable criteria of the sarcomatous picture. His method involved highly technical and painstaking work in order to make the actual count of mitotic figures upon which he based an estimate of the prognosis. Significantly he noted no gradual gradation in the number of mitotic figures and emphasized that sections of the tumors examined contained either (1) very many, (2) few, or (3) practically no mitotic figures. This finding has suggested to many observers that even a rough estimate of the frequency of mitotic figures would provide a practical means of judging the prognosis in an individual case.

In addition to evaluating the presence and number of mitotic figures, Evans described the appearance and significance of giant or atypical nuclei in myomas. He accepted Wilson's[17] observation that atypical or giant nuclear forms were evidences of amitotic division among degenerating cells. According to Evans, Wilson had shown that a division of the nuclear material might occur without a corresponding division of the cytoplasm. This process Wilson had interpreted as direct cell division, and he regarded it as an indication of degeneration in the cells involved. In discussing the significance of atypical or giant nuclei in fibroids Evans noted that bizarre nuclear forms had been reported in cultures of irradiated tissue in which similarly atypical nuclei appeared as degeneration replaced active proliferation.

Schmitz,[18] in 1941, described the prognostic significance of atypical and bizarre nuclear forms observed in repeated biopsies taken from cervical malignancy during the course of roentgen therapy. In Schmitz's material it was apparent that atypical or giant nuclei forecasting clinical arrest of the malignancy should be regarded as evidence not of proliferation, but of the degeneration of tumor cells. This interpretation of the significance of so-called giant or atypical nuclei seems equally applicable to similar atypical cells in degenerating myomas. At least in our material we have noted no evidence that such cellular irregularities

in myomas indicate a potentially malignant tumor. However, it must be emphasized that when similarly atypical cells appear in a tumor containing a noticeable number of mitotic figures a clinically malignant tumor should be suspected and a guarded prognosis given.

Our interest in sarcoma of the uterus was originally stimulated by observation of 2 patients whose malignant course was not predicted by the histology of the tumor removed. It seemed possible that other patients with equally malignant tumors might have been overlooked and their eventually malignant course not reported to us. With that possibility in mind we reviewed the histologic reports of 1,400 consecutive fibroids. Atypical cellularity was noted in 12 myomas, an incidence of 0.85 per cent, or one fibroid that might be viewed with suspicion in each 116 removed. Follow-up data on these 12 patients reveal that 11 have survived periods varying from eighteen months to over five years. Five have noted no signs of recurrent pelvic tumor during an interval of three to five years, while 4 have been perfectly well over five years. One of the 12 died two and one-half years after operation but no autopsy was held, and we could obtain no reliable information concerning the recurrence or absence of a pelvic tumor.

The records of the 12 patients showing atypical cellularity in fibroids have been added to the data of 3 similar cases reclassified nonmalignant in Table I. This combination provided us with a total of 15 patients to be regarded as borderline or potentially malignant fibroids. Obviously these 15 tumors were histologically atypical myomas and are not to be considered as sarcomas of the uterus. However, we have observed two patients develop a rapidly recurrent and clinically malignant tumor of the pelvis soon after removal of histologically benign but atypical myomas. In such instances routine histologic sections may have failed to portray a malignant picture that would have been apparent had more sections of the tumor being studied. Careful reexamination and additional sections would undoubtedly insure closer correlation of the histology and the clinical course. On the other hand, one purpose of this study has been to determine the reliability of routine histology in these doubtful or borderline cases. Tumors have been classified entirely on the basis of the pathologist's routine reports. On the basis of the follow-up data to be reported in Table III, we conclude that fibroids showing areas of atypical cellularity should not be viewed with alarm unless the histology warrants a diagnosis of established sarcoma.

Proposed Classification

Considering the data in Table II we were impressed by the relatively long survival of patients whose sarcoma was associated with a grossly appreciable fibroid. Seeking a practical basis for an estimate of the prognosis in an individual case, we have reclassified 60 patients into 4 groups as indicated in Table III.

TABLE III. PROGNOSIS IN ATYPICAL MYOMAS AND SARCOMA OF THE UTERUS

Study of 60 Cases: 45 Sarcomas of the Uterus, 15 Atypical Myomas Classified According to Suggested Grouping

GROUPS	TOTAL CASES	CASES LIVING	LENGTH OF TIME SURVIVORS FOLLOWED	DECEASED	LENGTH OF SURVIVAL
A Degenerating or soft rapidly growing myomas, atypical nuclei, or few mitotic figures	15	14	0—under 18 mo. 5—1½ to 3 yr. 5—3 to 5 yr. 4—over 5 yr.	1	2½ yr.
B Sarcomas associated with fibromyomas, atypical nuclei, and noticeable mitotic figures	14	10	1—under 18 mo. 0—1½ to 3 yr. 3—3 to 5 yr. 6—over 5 yr.	4	1—? 1—6 mo. 1—9 mo. 1—17 mo.
C Sarcomas in uteri not containing fibroids	28	4	0—under 18 mo. 1—2 yr. 1—12 yr. 2—14 yr. R	24	2—operative 11—1 to 3 mo. 4—3 to 6 mo. 4—6 to 12 mo.** 1—22 mo. 1—36 mo.* 1—?
D Carcinosarcomas, highly anaplastic undifferentiated cells (not two neoplasms combined)	3	0	—	3	1—? R 1—2 yr. R 1—2½ yr. R
Totals	60	28	—	32	—

Cases treated by radium without hysterectomy (R) or prior to hysterectomy (*) are indicated.

**Two of 4 cases, surviving six to twelve months, and *one case surviving thirty-six months, treated by radium before hysterectomy.

Group A includes rapidly growing soft myomas containing a noticeable number of mitotic figures, but with preservation of a fairly regular arrangement in spite of increased cellularity. In this group we would also place fibroids in which sections show atypical polymorphic or giant nuclear forms, usually in or adjacent to areas of degeneration in myomas. Fifteen patients in this group have been followed, 9 for over three years and 4 for over five years with no evidence to suggest that a clinically malignant tumor was overlooked at the time of operation.

Group B includes cases in which histologic section of a grossly appreciable fibroid reveals atypical nuclear forms *and* mitotic figures, evidences of the active proliferation of atypical cells. Twelve of these patients were noted in Table I as sarcomas associated with fibroids. Two additional cases, discovered in reviewing the histology of 1,400 fibroids, had not been properly filed in the record room and are included here as the thirteenth and fourteenth secondary sarcomas followed. Obviously Group B includes secondary sarcomas in myomas as well as primary sarcomas (belonging in Group C). We believe the majority of the clinically malignant tumors in this group are primary sarcomas associated with an incidental fibroid. For a practical estimate of the prognosis, if there was a grossly appreciable fibroid, we have placed the tumor in Group B.

Group C consists of tumors frankly sarcomatous arising in uteri not containing fibroids. It is evident that a majority of patients with a true primary sarcoma of the uterus consistently run a rapidly fatal course.

Group D comprises the small group of highly anaplastic tumors usually designated as carcinosarcoma. The literature regarding this particular group of tumors provides a comprehensive discussion of the various histologic pictures frequently classified as carcinosarcomas. Hoffman[19] has called attention to the rarity in which this picture is due to coexisting carcinoma and sarcoma in the same uterus. Handley and Howkins[7] emphasize the difficulties of accurate diagnosis in this group of cases. They advise consideration of the possible effects of (a) secondary infection, (b) previous irradiation therapy, or (c) sarcomatous infiltration of a secondarily invaded and distorted epithelial surface. At least two of the three cases in our series were in all probability highly malignant anaplastic carcinomas. They are included here because we wish to mention later the comparative radiosensitivity of these tumors compared to other types of uterine sarcoma.

We believe this proposed grouping provides a practical basis by which sarcomas of the uterus may be classified. Our observations suggest this grouping may prove an aid in estimating prognosis in the individual case. The relationship between prognosis and the proposed grouping is indicated in the following outline:

A. The presence of a noticeable number of mitotic figures in rapidly growing myomas or the finding of giant cells—atypical polymorphic nuclear forms, in or adjacent to degenerating areas in leiomyomas, may be regarded as criteria warranting a suspicion of sarcomatous change, but neither finding alone should imply a clinically guarded prognosis.

   Patients in this group should not be considered as harboring a malignant tumor and so-called prophylactic irradiation therapy is not justified.

B. Histologic evidence of actively proliferating atypical cells in patients with a grossly appreciable myoma—the presence of mitotic figures *and* atypical nuclear forms, warrants a diagnosis of sarcoma, arising either as a result of so-called sarcomatous degeneration in a fibroid or as a primary sarcoma associated with an incidental myoma.

   Patients in this group should be treated by radical surgery. A guarded prognosis should be given as recurrence or extension of a clinically malignant tumor may be expected in a definite proportion of these cases.

C. Histologic diagnosis of sarcoma in a uterus not containing fibroids usually foretells a rapidly fatal course irrespective of the type of predominating cell or the apparent histogenesis of the tumor. In a striking percentage of cases operative removal of this type of tumor is followed by death from vascular accidents during hospital convalescence. Preoperative irradiation may decrease the number of postoperative deaths due to thromembolism but the majority of primary sarcomas of the uterus are relatively resistant to irradiation therapy and usually only palliation can be expected.

D. Certain highly anaplastic tumors of the uterus are frequently classified as carcinosarcoma. In a majority of these cases the histologic picture indicates a highly malignant tumor difficult to classify rather than the presence of coexisting carcinoma and sarcoma.

Patients in this group provide the more radiosensitive of the tumors classified as sarcomas of the uterus, but early extension or local recurrence is the rule. Death due to metastasis may occur in spite of apparent local eradication of the tumor.

Conclusions

Fibroids showing areas of atypical cellularity should not be viewed with alarm unless the histologic changes justify a diagnosis of established sarcoma.

The prognosis of patients with sarcoma of the uterus primarily depends upon the state of the disease when adequate treatment is instituted. To a lesser degree prognosis varies with the histology of the tumor.

A comparatively simple basis for the classification of sarcomas of the uterus is suggested as an aid in estimating the degree of clinical malignancy.

A general attitude of pessimism is not justified in the management of patients with sarcoma of the uterus. Among the patients followed in this study and in a majority of similar reports in the literature, the percentage of five-year survivals is approximately 30 per cent.

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Discussion

DR. WILLIAM H. VOGT, St. Louis, Mo.—When Dr. Randall sent me his paper for review only a few days ago, I was immediately impressed with the large number of sarcomas of the uterus reported. His figures show that even when all sarcomas

of the uterus associated with fibroids are eliminated, 4.7 per cent of all malignancies of the uterus are sarcomas. Since the essayist's percentage seemed rather high, I investigated the records at our own hospital. Here I found that out of the last 391 cases of malignancy of the uterus there were 11 cases of sarcoma. Ten of these were sarcoma of the uterus proper, one of the endometrium, and there was no sarcoma of the cervix. Two of the sarcomas of the uterus were associated with fibroids. If we eliminate these two cases, as the author has done in his series, we then have a figure of 2.3 per cent. Unfortunately, time did not permit an investigation of the outcome of our recorded cases.

Classifications of sarcoma of the uterus vary greatly and are confusing. Dr. Randall attempts to establish criteria on which to base an estimate of the prognosis. I can, however, see little difference in his Group "A" and Group "B" cases. Included in both of these groups are tumors in which atypical polymorphic or giant nuclear forms appear in fibroids. In both groups mitotic figures are present. I am sure that no one would claim that the presence of mitotic figures was necessarily evidence of malignancy. A fibroid, for instance, having the appearance of a normal tumor except for a few more cells than usual and containing one or two mitotic figures to every 10 or 20 high power fields, should not be considered as a sarcoma but simply as a rapidly growing non-malignant tumor. If, however, the tumor is very cellular it might be looked upon as suspicious.

Considerable interest has lately been aroused by the degree of nuclear activity as indicated by the mitotic count. Evans and Kimbrough found, for instance, that the mitotic count parallels, as a rule, the degree of clinical malignancy. Novak relates his experience with the mitotic count and states that of 20 cases in which 0 to 5 mitoses were found in 20 fields, 15 were living more than 3 years after operation, 1 received only palliative treatment and presumably died, and 3 were not traceable. On the other hand in 7 patients with mitotic counts above 30 and up to 88, all are known to have died. He said: "It would therefore seem that when the mitotic count is low, recovery is the rule."

No one, I think, would argue with the essayist about his "C" and "D" groups. These are highly malignant tumors running a rapidly fatal course.

To attempt a classification as Dr. Randall has outlined is undoubtedly desirable, but I am wondering whether by this means we will be in any better position to grade the degree of malignancy of a given tumor. The old classification of spindle cell, round cell, and mixed cell and, perhaps, giant cell tumor is probably as satisfactory as any, remembering that the unripe or undifferentiated cells are the most malignant and the spindle cell type of the leiomyosarcoma with considerable differentiation is of the lowest grade of malignancy. This, coupled with an accurate mitotic count, will, in the majority of instances, answer our needs.

DR. EMIL NOVAK, BALTIMORE, MD.—Several years ago we reported from our laboratory a series of 59 cases of sarcoma of the uterus, with statistical results quite comparable to those reported by Dr. Randall. The gross appearance of a myoma will often justify the presumption of its benign or malignant nature. If the tumors are opened in the operating room, as they should be, and the cut surface is hard, glistening and whorl-like, one need have little fear of sarcoma. If, on the other hand, the cut surface shows a soft, pultaceous area, with often a ragged central cavity, one should at least suspect the existence of sarcoma. The common hyaline degeneration is more likely to present areas of amorphous, jelly-like appearance, with a tendency to the liquefying changes constituting cystic degeneration.

The mere fact that a sarcomatous uterus is nodular in appearance does not justify the conclusion that the sarcoma originated in myoma, because sarcoma arising in the uterine wall not infrequently grows in a nodular fashion. In other cases the growth is diffuse and more or less symmetrical. When the origin is in the endometrium, as it not infrequently is, it characteristically assumes a polypoid

pattern, the polypoid masses being bulky, infiltrative, and friable. The same thing is true of growths arising in the endocervix, so that if one removes a polyp which, instead of the fragile structure of most cervical polyps, is of this bulky friable structure, one should suspect sarcoma.

Diagnosis is ordinarily not made until, or even more frequently, after operation. Curettage may at times reveal the lesion preoperatively, but more often not. The microscopic diagnosis is often easy enough, but, as with other types of malignancy, there are borderline cases concerning which pathologists differ. In most of these cases this doubt is of very little practical disadvantage, as they are likely to be of a low degree of malignancy.

If the microscopic section shows the muscle cells uniform in size and nuclei, making due allowance for the differing angles of section of the muscle bundles, there is no justification for the diagnosis of sarcoma, no matter how cellular the growth. The criteria of malignancy here, as with sarcoma in general, are disparity in the size of the cells, and of the nuclei, with mitosis, hyperchromatosis, and other evidences of anaplastic activity. Giant cells are perhaps most often of the symplasmic variety, due to blending of the cytoplasm of adjoining cells in degenerating areas of the tumor. I agree with Dr. Vogt that in Dr. Randall's suggested classification, there is no reason for the separation of Groups A and B, both of which pertain to sarcoma originating in myoma, though the degree of malignancy may of course differ very widely.

DR. JAMES E. KING, BUFFALO, N. Y.—My interest in this subject arises from the fact that two of my patients form a part of Dr. Randall's report. One was the girl of 8 years who had a sarcoma butyroides. I told the parents that the outlook was very unfavorable, but the patient comes in to see me occasionally, still in very good health, now 19 years of age and is having normal menstrual periods. She has a perfectly normal pelvis.

The other case was a patient from whom I removed polyps every two or three months over a period of about a year and a half. These polyps were always reported by the pathologist as benign. Clinically these recurrent polyps were not benign and I felt that there was very definitely more than a suspicion of sarcoma. Later the uterus was removed and found to contain several additional polyps and several tumors that appeared to be fibromas. That was less than a year ago and the woman now has a large recurrence that occupies the entire pelvis and much of the abdomen.

The classification was primarily an attempt to find a distinction between Groups "A" and "B," and next to call attention to the purely clinical observation that sarcoma in association with fibroids is usually not a rapidly fatal tumor. On the other hand, the diagnosis of sarcoma when there is no fibroid confusing the histologic picture foretells a rapidly fatal course. The tumor may prove radiosensitive, and simply because sarcoma is included in the nomenclature of a neoplasm does not mean that irradiation may not be of benefit.

DR. RANDALL (closing).—I am afraid that I failed to make clear the distinction between Groups "A" and "B." Two pictures of atypical cellularity may be seen associated with myomas. In the first there are very atypical, giant or bizarre nuclear forms. Such atypical nuclei, usually noted in degenerating myomas, are not an indication of malignancy. Secondly, there may be impressive numbers of mitotic figures in rapidly growing myomas, but alone, mitotic figures are not an indication of malignancy. On the other hand, when sections of the uterus show strikingly atypical cells plus mitotic figures, such a combination spells sarcoma. In Group A there are atypical nuclei *or* mitotic figures, in Group B *both* atypical nuclei and mitotic figures. That was the distinction between tumors placed in Groups "A" or "B."

POST-PARTUM OBSERVATION OF PELVIC TISSUE DAMAGE*

HAROLD L. GAINEY, M.D., KANSAS CITY, MO.

THESE cases chosen for report represent the last 1,000 patients examined in the postnatal clinic of the obstetric and gynecologic department at the University of Kansas. The primary objective in this study was the teaching of gynecologic anatomy to graduate and undergraduate students. The need for this is readily recognized because of the limited number of female specimens in the anatomy department and, following this, only in the rarest instance is there any further possibility for study. It therefore remains that the clinic and operating rooms are the only places providing this opportunity.

Intelligent management of the obstetric patient with preservation of tissues and reconstruction of damage demands a knowledge of the structures. Simultaneously, observations were recorded and are now presented in the form of a preliminary report.

Three definite anatomic planes are of recognized importance, and damage may be observed in an objective manner. The upper pelvic floor is made up of the parametrial fascia with its localized condensations forming the uterosacral, Mackenrodt's ligaments and the much weaker cervicopubic fascia. Damage to this plane is manifested by cystocele, uterine descensus, and enterocele.

The pelvic diaphragm consists of the pubococcygeus, ileococcygeus and coccygeus muscles with their envelope of endopelvic fascia. Damage to this plane was recorded by palpation of areas of detachment, or atrophy, of the first two, relaxation of the introitus after voluntary effort at closure, and detachment of the urethra from its retropubic position.

According to Curtis and Anson it is the pubococcygeal division of the levators ani that affords continuous support for the organs of the urogenital and pelvic parts of the perineum; the iliococcygeus completes the diaphragm at the sides and behind but does not come in contact with the viscera.

The third plane, the urogenital trigone, closing the anterior triangle of the bony outlet with its fascial planes and musculature inclusions, is one of the areas most vulnerable to damage due to parturition. Damage to this plane was recorded by noting relaxation of the vestibule, detachment of urethra and by comparing with normal the "anovaginal" portion as determined by digital rectal examination. In addition to these planes of tissue structure, other injury occurs which is of vital importance to the patient's welfare.

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The attachments of the vaginal tube laterally and posteriorly to the endopelvic fascia covering the levators ani, the cervicopubic fascia anteriorly, the cul-de-sac peritoneum and uterosacral ligaments posteriorly, Mackenrodt's ligaments at each lateral fornix and finally to the vaginal portion of the cervix—all are extremely vulnerable to detachment.

The importance of a normal relationship between the vaginal walls and paravaginal supporting tissues has long been recognized. Mengert concluded following his experiments on cadavers, "that the paravaginal supports are fully as important as the parametrial, if not more so, in uterine support." Damage to the vagina is reported as detachment from specific areas or obliteration of fornices.

Vesical and anal sphincter damage was recorded as incontinence; congenital defects were eliminated. There were 20 in the group of 461 primiparas and 32 in the 539 multiparas who gave a history of incontinence either continuously or on lifting or coughing.

Anal sphincter incontinence was not encountered in 5 patients with third-degree laceration and repair. Much damage no doubt occurs to fascial planes not easily observed or recorded. The anterior compartment of the ischiorectal space which adds support to the pelvic diaphragm most certainly is damaged in each case as is true of the superficial perineal structures.

It must be made clear that the intent of this paper is to record tissue damage due to parturition as interpreted by postnatal examination. Consecutive cases were studied without regard for correction due to age, race, size of baby, bony pelvis, or method of delivery. These factors have been recorded and will be added at a later date in larger groups.

Material

Two main groups, multiparas and primiparas, were divided into three divisions. First, those delivered without apparent laceration. There were 456 multiparas and 209 primiparas in this group. Second, those delivered with laceration and repair, there being 109 primiparas and 61 multiparas. And third, those with episiotomy and repair. There were 143 primiparas and 22 multiparas in this group. Those delivered with laceration and repair were segregated for the obvious reason that some of the damage sustained might have been corrected by the repair.

Review of the damage observed in the entire group reveals parturition as a destructive process. Three hundred and thirteen (31 per cent) of patients suffered damage with resultant atrophy or detachment to the levators ani, varying from partial to complete damage of one or more components, the pubococcygeus being most vulnerable. One hundred and seventy-eight (18 per cent) manifested detachment of the urethra from its normal retropubic position indicating damage to that portion both of pelvic diaphragm and urogenital trigone. Three hundred and eighty-nine (39 per cent) had gaping of introitus when relaxed, and of these, 143 (14 per cent) remained gaping when voluntary effort at closure by levators was observed. Two hundred and thirty-five (24 per

cent) showed what was arbitrarily set as less than 60 per cent of normal height or thickness of the anovaginal portion of the urogenital trigone. Only those having less than 60 per cent were chosen because of the difficulty in establishing a normal. For this reason the percentage suffering injury is much less than actually exists, as this is one of the most frequently damaged areas. Episiotomy offers greatest protection to this area as will be seen when the two groups of primiparas with episiotomy and those delivered without apparent laceration are compared.

Difficulty was encountered in accurately recording damage to vaginal wall attachments; yet, its importance is great.

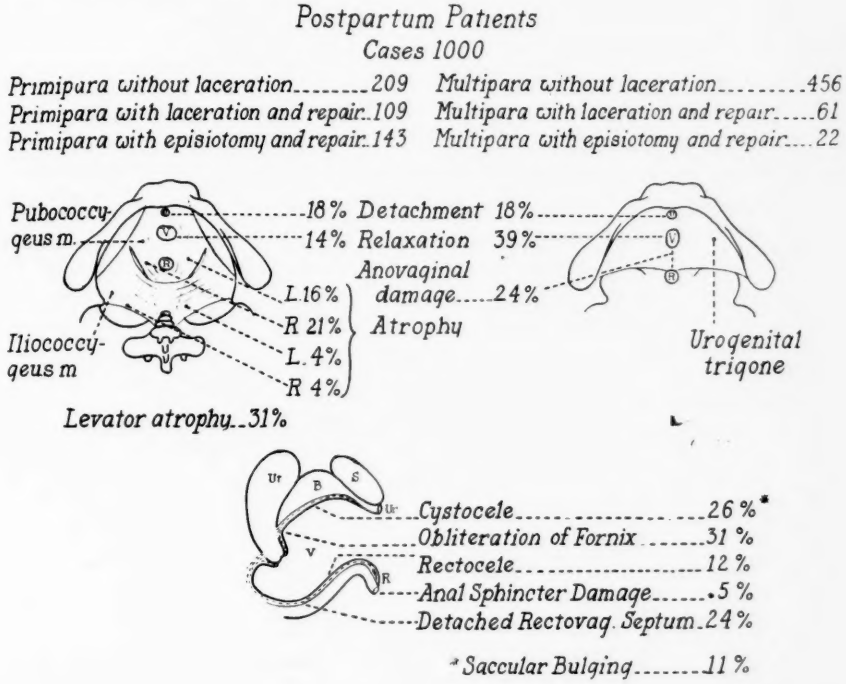

Fig. 1.

Two hundred and thirty-six (24 per cent) of the patients showed detachment of the vaginal wall from the endopelvic fascia on either side of the rectum and actual rectocele recorded in 120, or 12 per cent. Diffuse detachment or prolapse was noted in 202, or 20 per cent. Obliteration of the anterior fornix was partial to complete in 311, or 31 per cent. Cystocele as interpreted by definite saccular or diffuse bulging of anterior vaginal wall was present in 264 patients, saccular bulging being 11 per cent of total. Enterocele was not observed.

Nine instances of uterine descensus were observed, and in only one was it complete, all being in multiparas.

A comparison without the corrective factors mentioned is not justified but nevertheless it was interesting to note the like percentages of damage in the 3 groups of primiparas, the exception being in the "anovaginal" portion of the urogenital trigone in which case those with episiotomy and repair were benefited. The groups of multiparas are too small for com-

parison. When the two groups, multiparas and primiparas, are compared, it is apparent that multiparity increases tissue damage in a great degree to all areas except the levators, where it occurs to a lesser degree.

An exposition of the damage in the various groups and areas can best be seen in the illustrations (Figs. 1 to 7) and Tables I and II.

Multipara Without Laceration
Cases 456

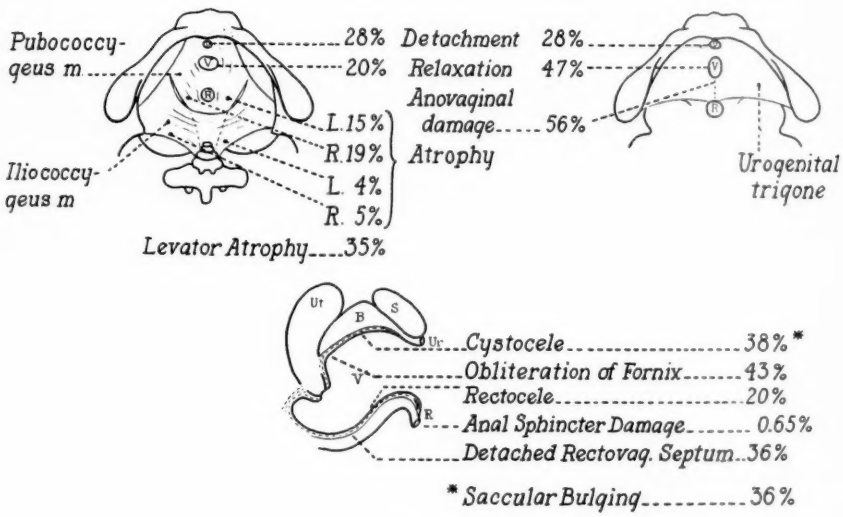

Fig. 2.

Multipara With Laceration and Repair
Cases 61

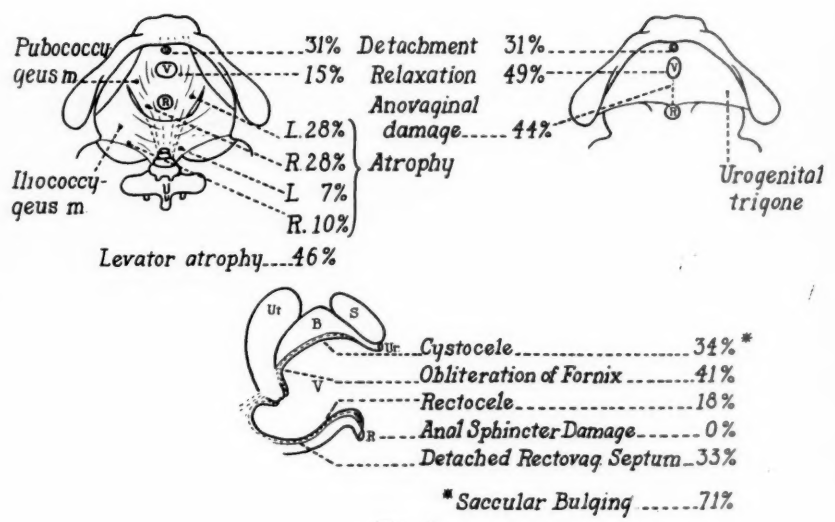

Fig. 3.

Multipara With Episiotomy and Repair
Cases 22

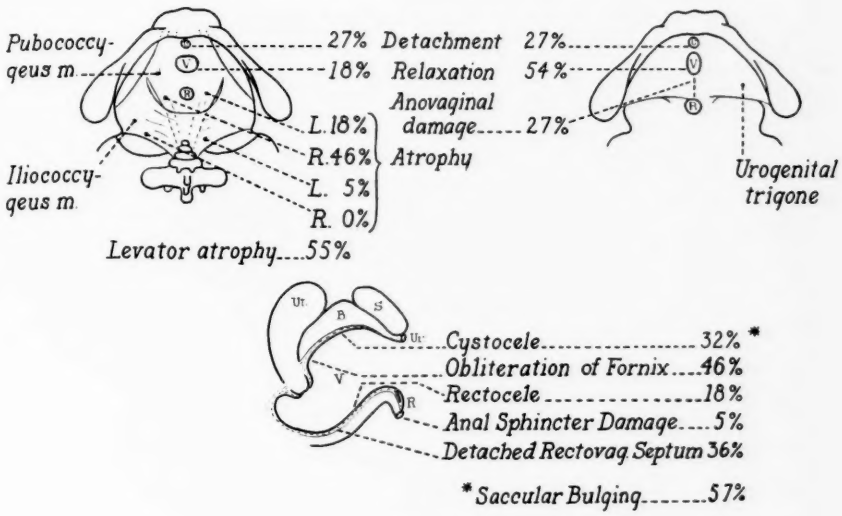

Fig. 4.

Primipara Without Laceration
Cases 209

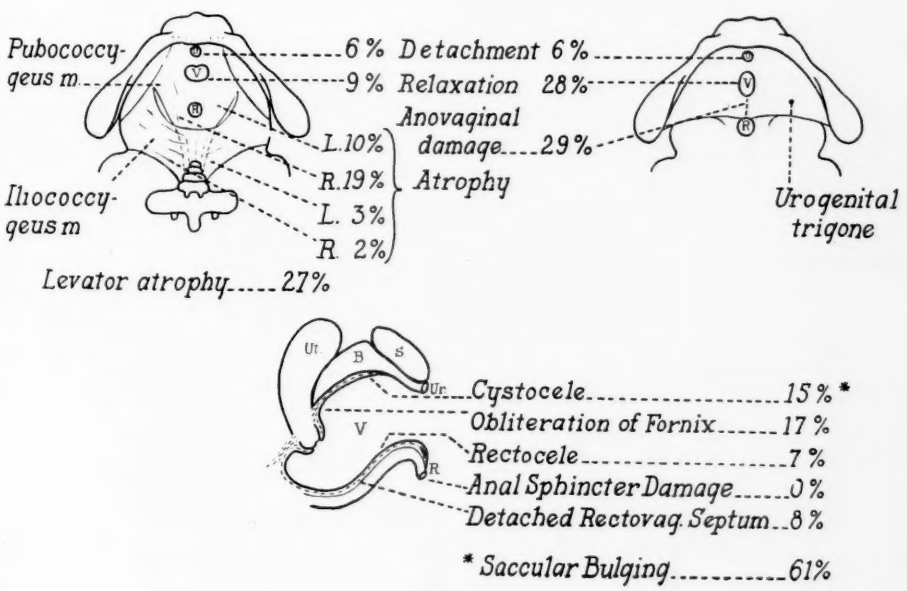

Fig. 5.

Primipara With Episiotomy and Repair
Cases 143

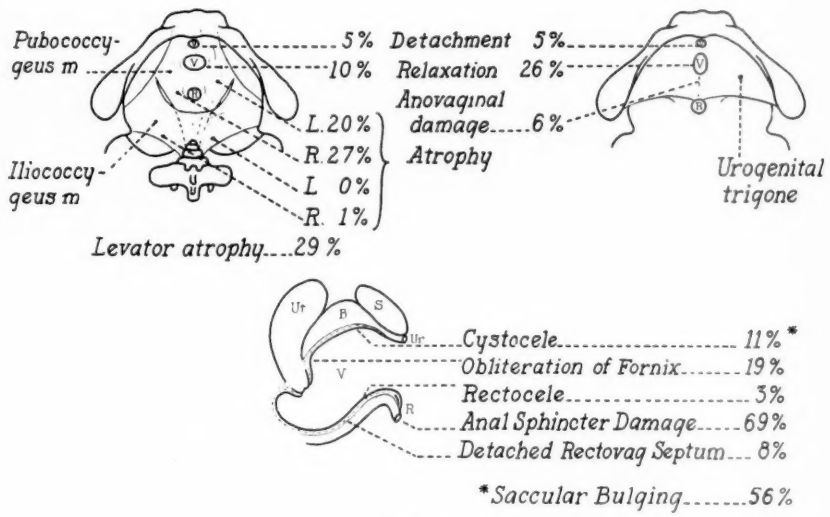

Fig. 6.

Primipara With Laceration and Repair
Cases 109

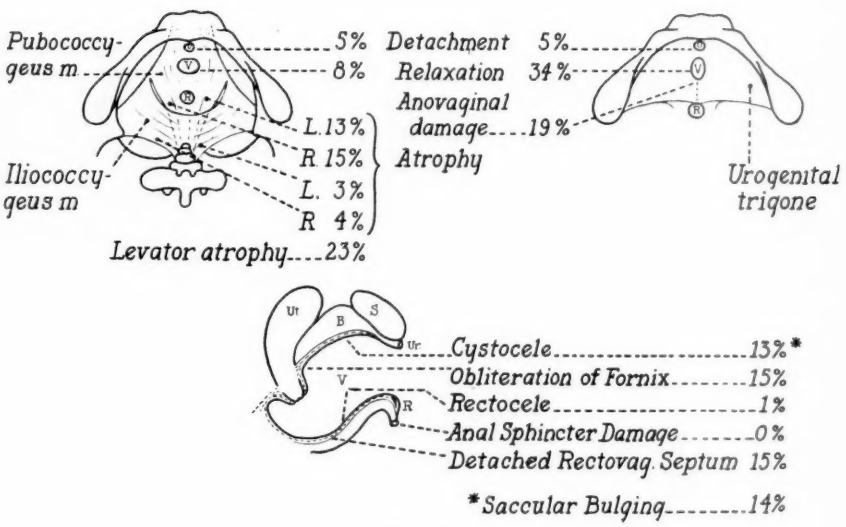

Fig. 7.

TABLE I. COMPARISON OF DAMAGE

	MULTIPARAS 539	PRIMIPARAS 461
Rectocele	19%	3%
Rectovaginal septum detachment	35%	9%
Prolapse vaginal walls	28%	10%
Obliteration anterior fornix	43%	17%
Cystocele { Saccular / Diffuse	38% { 15% / 85%	13% { 6% / 94%
Urethral detachment	28%	5%
Anovaginal trigone damage	53%	20%

TABLE II. COMPARISON OF LEVATOR DAMAGE

	MULTIPARAS 539	PRIMIPARAS 461
L. Pubococcygeus m.	17%	14%
R. Pubococcygeus m.	21%	20%
L. Iliococcygeus m.	5%	3%
R. Iliococcygeus m.	5%	2%
Total levator damage	37%	29%
Retrodisplacement	21%	21%

Summary

A method employed recording in an anatomical order pelvic tissue damage due to parturition is presented with a preliminary report of figures showing damage to the various planes and regions. Hazards in accurately observing damage are recognized, particularly of vaginal wall detachments, cystocele and rectocele. Subinvolution constitutes the main hazard and an effort at correction was made.

Conclusions regarding the controversial subject of routine episiotomy were avoided at this time because of an insufficient number of cases. Suffice it to say that both those with and without episiotomy suffered damage. Protagonists of either procedure need more detailed and objective evidence in order that unified thought and practice may benefit the parturient woman.

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1103 GRAND AVENUE

Discussion

DR. THADDEUS L. MONTGOMERY, PHILADELPHIA, PA.—I have read of these structures in books of anatomy, I have seen some of them in dissection, but I have never before realized that it is possible to identify these individual injuries and defects in anatomic structure in the puerperal patient. I am convinced that this very thing has been done by Dr. Gainey and that this very excellent paper is a record of patient and laborious achievement. I have thought over this paper many times, and now as I correct my discussion of it, I feel convinced that this presentation is an important contribution to obstetric and gynecologic literature.

I am of the impression that our results, where episiotomy has been employed during the delivery of the primigravidous patient, have been somewhat better than those described by Dr. Gainey. In this observation I may be entirely wrong and perhaps more detailed study of our own cases would indicate such. However, with the free use of median episiotomy, extended when necessary off to the side of the anus and the rectum, we have been able to avoid extensive urogenital trigone damage. In fact, I think the main indication for episiotomy is to prevent pressure of the head against the bladder, the urethra, and the fascial structures of the urogenital diaphragm.

To accomplish this with episiotomy, certain principles must be kept in mind: (1) Episiotomy must be performed early and before the head has greatly distended the lower birth canal; (2) episiotomy must be free (we prefer a median incision down to the sphincter and then an extension to the left of the sphincter toward the ischiorectal fossa); (3) the repair of this incision must be conducted with just as great care as a gyneplastic operation, which means that the field must be cleared of blood, must be properly exposed, and the procedure done in an orderly anatomic fashion; (4) the use of fine grades of catgut, notably 00 chromic catgut which we formerly used. There is very little tension in this area and all that one needs is material of sufficient tensile strength to hold the tissues together.

Where I find the greatest degree of damage of fascial structures and underlying muscle tissue is in the slender primipara who has a rapid, almost precipitous labor. Here, as Dr. Gainey has pointed out, damage of the urogenital diaphragm occurs, submucous injuries of the pubococcygeal portion of the levator ani muscle, rupture of the true ligaments of the uterus and a resulting early tendency to cystocele, rectocele, and descent of the puerperal uterus. While the slow, difficult labor of the less feminine type of patient may be more worrisome to the obstetrician, generally there is better recovery from tissue damage.

Finally, from the study of Dr. Gainey's paper, I am convinced that there is more to the examination of the postnatal patient than I have been practicing and I shall go back to this phase of our obstetric work with a renewed interest; thanks to this stimulating presentation.

DR. L. A. CALKINS, KANSAS CITY, KAN.—Assumption of damage in some of these areas, particularly in the anovaginal region, may easily be a matter of personal opinion. In order that his data be as accurate as possible Dr. Gainey did 500 of these patients and then discarded this group before reporting 1,000 cases examined since that time. I think there can be little question as to the accuracy of the damage reported in this study.

None of us has learned how to examine the pelvis completely and this presentation is perhaps a beginning in that direction. When we have learned to do this we will perhaps be in a position to determine whether a woman should have an episiotomy or not.

DR. A. J. RONGY, NEW YORK, N. Y.—I agree with Dr. Calkins that most of us do not know how to examine the pelvis and that we do not understand its anatomic construction. E. K. Roberts has probably made the most extensive study of the soft structures of the pelvic floor. He concluded that the uterus is held in position at a fixed point in the pelvis, slightly above the internal os, by a diaphragm composed of connective and muscular tissue and their blood vessels. It is these structures, or the upper diaphragm, as he terms it, which when injured during labor cause the uterus to be dislocated from the fixed position.

The mechanism which injures the lower structures of the soft pelvis largely depends upon the construction of the bony outlet of the pelvis. If an imaginary line is drawn across the ischial tuberosities, the pelvic outlet is divided into an anterior

and a posterior segment. The anterior segment normally measures about 9 cm., the posterior segment about 7 cm. Now, if the anterior segment of the outlet is contracted because of some peculiar formation of the pubic arch, the child will have to be born at a greater expense to the posterior segment, and therefore more damage will result to the soft parts of this segment and perineal lacerations are likely to be more extensive. However, if the posterior segment is contracted, the child is born at the greater expense of the anterior segment, and then the injuries will be more extensive in the anterior vaginal wall and result in a greater incidence of cystocele formation.

Marion Sims long ago observed that complete lacerations of the perineum very seldom were accompanied by cystocele. The reason for it was not well understood at that time.

The configuration of the outlet of the bony pelvis has a practical bearing on the management of a case in labor. Whenever there is an evident contraction of the posterior segment of the outlet, a thorough "ironing out" of the soft tissues or an episiotomy should be done before the tissues are too greatly damaged. Conversely, if the fetal head promises to deliver at the expense of the anterior segment, episiotomy is hardly necessary, because the injury to the soft parts of the posterior segment is less likely to occur.

In order to make this study more complete, Dr. Gainey will have to go a step further and investigate the position of the fetal head and correlate it with the injuries to the pelvic floor. Obviously, occipitoposterior is likely to induce greater damage to the structures than occipitoanterior position. Again the duration of labor is likely to be a factor in the production of injuries to the soft parts.

DR. LOUIS E. PHANEUF, BOSTON, MASS.—Dr. Gainey's presentation stresses the importance of postnatal care which has come into use later than prenatal care and which is one of the great advances in obstetrics. The amount of injury should be determined immediately after labor, and not some months later, when the woman presents herself as a gynecologic patient. In this series, the damage to the pubococcygeal muscles has been greater than I had supposed it ordinarily to be.

This brings up a practical point which is that in subsequent repair, the approximation of the crura of the pubococcygei muscles, to narrow the genital hiatus, is very important. One would, however, not expect to diagnose an enterocele at such an early examination, as this occurs in the course of time through abdominal pressure directed against a deep cul-de-sac of Douglas.

Another point is gained from this presentation, namely that if we expect to get satisfactory results from our repair operations in gynecology, we must do them before these important muscular and fascial structures have undergone too marked atrophy. If the repair is done early, before the atrophy has become too pronounced, we should expect fewer recurrences.

DR. GEORGE F. PENDLETON, KANSAS CITY, MO.—This presentation is not only an argument for or against episiotomy. It points out all of the damage that a normal labor produces. This damage is practically all second stage damage—a part of the labor which we, with the exception of Dr. Potter, accept. This calls particular attention to the need of watching for the full bladder at the time of full dilatation of the cervix. It points also to a lot of questions, such as analgesia or anesthesia in the second stage, or perhaps the stimulation of labor pains.

DR. GAINEY (closing).—Our goal is to apply in our work practical interpretations, but to date this objective has been overshadowed by an effort to develop a method of analysis of soft tissue damage due to parturition. As the number of cases in the individual groups becomes larger, conclusions as to methods of min-

imizing damage will, we hope, be forthcoming. To date it does not seem that episiotomy offers a guarantee against damage to the levators but that the trigone is protected. The attachments of the vagina by its paravaginal adventitious tissue to the heavier fascial structures of levators and upper pelvic floor are protected from unnecessary distention and elongation by incision of the perineal outlet.

Our interpretation of damage to levators, if correct, suggests a possibility that it is irreparable from a reconstructive standpoint although not necessarily serious in its limitation of normal pelvic diaphragm function. Interpretation of damage to the upper pelvic floor apparently must wait for senility to make itself manifest in the majority of cases other than those of congenital defects.

The most serious and permanently disabling damage on the functional side in reasoning from our present observations is not to the levators or trigone but from detachment of the vaginal tube from its paravaginal attachments.

A REPORT OF THE CESAREAN SECTIONS DONE AT THE PHILADELPHIA LYING-IN-PENNSYLVANIA HOSPITAL*

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(From the Philadelphia Lying-in-Pennsylvania Hospital, and the Gynecological Department of the Jefferson Medical College)

THE present Philadelphia Lying-in-Pennsylvania Hospital was opened on July 1, 1929, and, up to March 1, 1942, 27,829 babies were delivered in the institution. The operative incidence for all deliveries was 63.2 per cent, when all but spontaneous births were considered operative deliveries. The maternal mortality for the period from July 1, 1929, to March 1, 1942, was 0.4 per cent for all deliveries and in the last one and one-half years, it was slightly less than 0.2 per cent. The neonatal and stillbirth rate has been 5.3 per cent and the corrected infant mortality rate has been 2.5 per cent for an eleven-year period ending in January, 1942. In the last one and one-half years, the infant mortality rate has been 3.1 per cent without correction.

This report includes all the cesarean sections done at the Philadelphia Lying-in-Pennsylvania Hospital in Philadelphia during the ten-year period from July 1, 1932, to July 1, 1942. This period was chosen because it would include the work at the institution during the current period and the constant work of a group of obstetricians, over two five-year periods.

The cesarean sections noted in this report have been done under the direct supervision of some member of the attending staff. In many instances a senior member of the staff would assist a junior member of the attending staff or a house officer. The aim of the whole organization has been to allow men to qualify themselves by experience, but until their competence was proved they were not given the responsibility of working without adequate supervision of one of the better trained men. This rule has applied to private as well as ward cases, and has been adhered to very closely. In most instances the cesarean sections have been done after the necessity for the operation was agreed upon by

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more than one member of the staff. This report represents the work of a group of men working as a unit to do what in their judgment seemed best at the time.

TABLE I. INCIDENCE OF CESAREAN SECTION

	DISTRIBUTION OF CASES			CESAREAN SECTIONS		
	TOTAL ADMISSIONS	PRIVATE	WARD	TOTAL	PRIVATE	WARD
Ten-year period 7/1/32 to 7/1/42	22,754	8,190	14,564	1,322 5.8%	785 9.58%	537 3.6%
First five-year period 7/1/32 to 7/1/37	11,445	3,188	8,257	665 5.8%	325 10.2%	340 4.2%
Second five-year period 7/1/37 to 7/1/42	11,309	5,002	6,307	657 5.8%	460 9.2%	197 3.1%
One and one-half-year period 1/1/41 to 7/1/42	3,307	1,748	1,559	187 5.66%	133 7.6%	54 3.4%

Table I shows the distribution of cases on the private and ward services over the whole ten-year period. This ten-year period is analyzed in two five-year groups designated as the first period from July 1, 1932, to July 1, 1937, and the second period from July 1, 1937, to July 1, 1942. The distribution of cases is also shown for the period from Jan. 1, 1941, to July 1, 1942, to show better the current distribution of cases, and the incidence of operation. During the whole period there were many more patients on the ward service than on the private service. During the second five-year period the ratio of ward patients to private patients changed and during the last one and one-half years there have been more patients treated on the private service.

During the whole ten-year period, 1,322 cesarean sections were done, 785 operations, or an incidence of 9.3 per cent, were done on the private service and 537, or an incidence of 3.6 per cent, were done on the ward service. Fortunately for comparison the number of operations were about the same during both five-year periods, and the incidence of operation, 5.8 per cent, was the same for both periods.

The incidence of cesarean sections for the whole group is higher than many reports studied and is about twice the incidence occurring in the whole Philadelphia area as reported by the Committee on Maternal Welfare of The Philadelphia County Medical Society for a comparable time. The incidence of the operation on the ward service, however, corresponds closely to the reports given from other institutions.

The incidence of cesarean sections on the private service for the first period was 10.2 per cent, and for the second period it was 9.2 per cent, and for the period from Jan. 1, 1941, to July 1, 1942, it was 7.6 per cent. The incidence is high because of the selected group of patients which are referred to the hospital, particularly on the private service, and because of the liberal view taken by the staff toward the operation. The view taken by the staff is that when sections are indicated and performed by experienced gynecologic and obstetric surgeons it is a relatively safe and satisfactory procedure for the patient and for the physician.

Table II shows the obstetric histories of the patients for the whole series of 1,322 cases, and for the two five-year periods. A parity of more than two is not specified because it has no particular significance in this report. Most of the patients were primiparas and secundiparas, because

the policy of the staff of the hospital is to give all patients the opportunity for sterilization at the time of the second cesarean operation. The ratio of primiparas to multiparas has changed considerably over the two periods, because during the second period more patients came to the hospital because of accidents which had occurred with the first pregnancy and labor which had terminated in the death of the child.

TABLE II. OBSTETRIC HISTORIES OF PATIENTS

	PRIMIPARAS	SECUNDIPARAS	MULTIPARAS (2+)
Total number of cases 1,322	508 38.4%	419 31.7%	395 30.0%
First period, 7/1/32 to 7/1/37 665	334 50.2%	185 27.8%	136 20.5%
Second period, 7/1/37 to 7/1/42 657	174 26.5%	237 36.0%	246 37.4%

Table III shows the chief indications for section for the whole period and the first and second periods. The indications are the usual ones in most instances, the main ones being disproportion and previous section. The totals of these two indications are about the same for both periods, being 65.2 and 61.0 per cent, respectively. This occurred because a previous cesarean section was usually considered a definite indication for a subsequent operation without proving that a disproportion did, or did not, exist. Disproportion, which is relative, occurred frequently in this

TABLE III. CHIEF INDICATIONS FOR OPERATIONS

	WHOLE GROUP	FIRST PERIOD	SECOND PERIOD		WHOLE GROUP	FIRST PERIOD	SECOND PERIOD
Totals	1,322	665	657	Uterine inertia	8	7	1
Disproportion	534 40.4%	315 47.5%	219 33.3%	Ovarian cyst	7	4	3
Previous cesarean section	299 22.2%	117 17.7%	182 27.7%	Brow or face presentation	4	3	1
Placenta previa	84 6.4%	40 6.0%	44 6.7%	Bicornate uterus	4	3	1
Toxemia	66 5.0%	43 6.5%	23 3.5%	Obtain living child	3	2	1
Premature separation	46 3.4%	19 3.0%	27 4.1%	Acute appendicitis	3	2	1
Heart disease	36 3.5%	19 3.0%	17 2.2%	Uterine rupture	5	2	3
Fibroids	35 3.3%	13 2.0%	22 4.0%	Tuberculosis	4	2	2
Cervical dystocia	33 5.2%	10 1.5%	23 4.0%	Post mortem to save baby	3	1	2
Previous vaginal repair	24 2.2%	9 1.5%	15 2.1%	Abdominal pregnancy	2	1	1
Elderly primiparas	19 1.4%	14 2.0%	5 0.8%	Pyelonephritis	8	0	8
Transverse lie	10	4	6	Imperforate anus opening into vagina	1	0	1
Sterilization	8	6	2	Unclassified. Not of obstetric importance	76	29	47

group of patients, and its existence may be a question by some. Placenta previa and premature separation of the placenta was regarded as an indication for cesarean section in almost all instances where it occurred and the incidence was about the same during both periods. Toxemia had become a much less frequent indication for cesarean section in the second period and indicates plainly the reduced incidence of the malady and the change in the management of the condition. The other indications have occurred infrequently and in some cases the procedure in management may not seem to be the one that would be chosen by some.

Table IV lists the types of cesarean sections which were done during the ten-year period and during the first and second five-year periods. During the whole period of this report, 71.84 per cent of the patients had classical operations and there were slightly more of the classical operations in the second period than in the first. In most large clinics the tendency has been for the low type operation and it is rather interesting to observe that the incidence of the low type operation had diminished

TABLE IV. TYPES OF CESAREAN SECTIONS

	TOTAL	CLASSICAL	KERR	BECK	PORRO	WATERS	NOT STATED	STERILIZATION
Ten-year period 7/1/32 to 7/1/42	1,322	949 71.8%	256 19.4+%	68 5.1+%	34 2.5+%	2	13 1%	408 30+ %
First period 7/1/32 to 7/1/37	665	461 71.1%	127 19.0+%	53 8.0+%	14 2.0+%	0	10 1.5+%	178 27.0%
Second period 7/1/37 to 7/1/42	657	488 74.3+%	129 20.0+%	15 2.3+%	20 3.0+%	2	3	230 35.0%

rather than increased during the second five-year period. For a period of one year, during 1936 and 1937, the Kerr type operation was done almost routinely. The results during that year showed no variation from the results which had been secured previously and for that reason the tendency seemed to be toward fewer low type operations. The attitude of the staff now toward low sections seems to be that patients who have been in labor over twelve hours and patients with ruptured membranes or potential infection should have a low type cesarean section or a Porro type operation. In perfectly clean and elective cases, it is thought unnecessary to do anything more than a classical operation. Most sterilizations were done on patients who had had more than one cesarean section and the method used for sterilization was the Pomeroy modification of the Madlener operation.

Table V shows the time and the number of patients who were in labor and the number of patients with ruptured membranes. Usually an effort was made to avoid a cesarean section after rupture of the membrane, and this accounts for the few patients who were operated upon after the membranes had ruptured. This attitude is demonstrated very clearly

TABLE V. RECORD OF LABORS

LENGTH	PATIENTS IN LABOR		MEMBRANES RUPTURED	
	FIRST PERIOD	SECOND PERIOD	FIRST PERIOD	SECOND PERIOD
1-12 hours	107	109	42	44
12-24 hours	64	43	5	25
24-48 hours	34	27	5	12
48+ hours	5	11	8	4

in the table when it is observed how few patients had ruptured membranes for a period longer than twelve hours. Rupture of the membranes has been considered an absolute indication for a low cesarean section or a Porro operation, depending upon the length of time over which the membranes have been ruptured and the evidence of infection.

Table VI is a study of temperature morbidity during the second period of this report. Until April, 1940, our standard of temperature morbidity was a "temperature of 100° F., or over, twice in any twenty-four hours excluding the first twenty-four hours after delivery, operation, or admission." With this standard as a basis, the temperature morbidity was 59 per cent. The new standard for temperature morbidity is the one recommended by the Maternal Welfare Committee, and, since its adoption, there have been 245 patients delivered by cesarean section with a temperature morbidity of 22 per cent, which is within expected and normal range. The patients operated upon during the first period of this study were not included in this table, because it was thought that they would show nothing according to the present standards of morbidity.

TABLE VI. STUDY OF TEMPERATURE MORBIDITY (SECOND PERIOD)

	OLD STANDARD	NEW STANDARD
Total patients operated upon	412	245
Total morbidity	247—59.0%	54—22.0%
Causes of morbidity		
Postoperative reaction	128—30.0%	22— 9.0%
Endometritis	35— 8.7%	14— 6.0%
Sapremia	23— 5.5%	1— 0.5%
Wound infection	8— 2.0%	5— 2.0%
Pyelitis	35— 8.7%	6— 2.4%
Pneumonia	8— 2.0%	3— 1.2%
Phlebitis	8— 2.0%	0—
Breast engorgement or infection	2— 0.5%	3— 1.2%

Table VII shows the maternal mortality for the various periods on the private and ward services. For the entire group of 1,322 patients, there were 26 maternal deaths, or an incidence of 1.96 per cent. During the first period, there were 17 maternal deaths, or an incidence of 2.55 per cent. During the second period, there were 9 maternal deaths, or an incidence of 1.37 per cent. During the periods compared, there was little change in the maternal mortality on the ward service, but there was a marked drop in the maternal mortality on the private service. The patients having cesarean section on the private service from July 1, 1942, numbered 460, with 3 maternal deaths, or an incidence of 0.65 per cent. It is difficult to explain the rather high incidence of 3.0+ per cent of ma-

TABLE VII. MATERNAL MORTALITY

NUMBER OF CASES	PRIVATE	DEATHS	WARD	DEATHS	TOTAL DEATHS
1,322 7/1/32 to 7/1/42	785	9 1.15%	537	17 3.17%	26 1.96%
First period 665 7/1/32 to 7/1/37	325	6 1.84%	340	11 3.23%	17 2.55%
Second period 657 7/1/37 to 7/1/42	460	3 0.65%	197	6 3.00%	9 1.37%

ternal mortality on the ward service, and one can conjecture as to why they occur, but all the explanations do not hold in each instance. When these deaths are analyzed more carefully we may find an explanation.

Table VIII shows a tabular analysis of the 26 maternal deaths. Sixteen deaths, or a mortality of 1.67 per cent, followed 949 classical operations; 5 deaths, or a mortality of 11.7 per cent, followed 34 Porro operations; 3 deaths, or a mortality of 1.19 per cent, followed 256 Kerr operations; and two deaths, or a mortality of 3 per cent, followed 68 Beck operations. During the first period there were 6 deaths, due to shock and in the second period there were 5 deaths due to shock, a total of 11. Six of these 11 deaths were apparently accidents which occurred and could have been prevented. The operation, however, was the factor which was accepted as the cause of death, but one cannot be sure that the anesthetic, which was gas and ether in each instance, was not the responsible factor.

Three of the 11 patients who died of shock had either placenta previa or premature separation, one had a ruptured uterus, and one died during cesarean section following a traumatic attempt at vaginal delivery. The type of operation seemed to have no bearing on the outcome.

During the first period there were 4 deaths from peritonitis and one from peritonitis and pulmonary embolism, and during the second period there was 1 death from peritonitis. Two of the deaths from peritonitis followed the Porro operation, 3 followed the classical, and one followed the Kerr operation.

Pulmonary embolism accounted for 3 deaths, one of these noted above had peritonitis, and cerebral embolism accounted for one death.

There were 3 post-mortem cesarean sections: One patient died of Avertin anesthesia before the operation was begun and a post-mortem cesarean section was done in an effort to save the baby. Another patient died of bronchopneumonia about six weeks before term. A third patient died of placenta previa two and one-half weeks before term, and a post-mortem section was done to save the child, without success.

One patient died of eclampsia and convulsions twenty-four hours after delivery by cesarean section, because it was thought immediate delivery was necessary.

One died of pneumonia and nephritis after delivery; the nephritis had been present when pregnancy occurred, and she had had a previous section.

Another patient died of pneumonia on the fifth postoperative day.

When these deaths are analyzed according to the standard suggested by Schumann, we find that 9 of the patients died from causes complicating pregnancy and labor, or other systemic conditions, and that the method of delivery could not have been a factor in the cause of death. There are many interesting data which can be discussed in regard to the maternal mortality which occurred among these patients. Some of these deaths should not have occurred, and in retrospect and in staff conferences, where they were always discussed critically, the errors, when they existed, were attributed to the responsible person. These deaths were also analyzed by the Philadelphia Maternal Mortality Committee and the factor responsible for the cause of death was determined.

As others have said, and it seems to be pertinent here that a study of maternal mortality connected with cesarean section or a critical attitude toward the high incidence of cesarean section will not change the judgment of an individual when he is faced with the decision of how best to try to save the life of a mother and a child. The training, experi-

TABLE VIII. ANALYSIS OF DEATHS

YEAR	SERVICE	AGE	PARA	PREV. C. S.	INDICATION	TYPE C. S.	LABOR	MEMB.	EXAM.	ANES.	CAUSE OF DEATH	WEIGHT OF CHILD	SEX OF CHILD	CHILD RESULTS
First Period														
1932	P	22	i	0	Contracted pelvis disproportion	B	5½ hr.	0	2 Vag.	G & E	Post-partum shock and collapse	8-3¼	F	Lived
1933	P	29	i	0	Myoma uteri, toxemia disproportion	C	0	0	1 Vag.	G & E	Peritonitis, pulmonary embolism	6-0	F	Lived
1934	W	34	iv	3	Chronic nephritis, previous C. S.	C	0	0	0	E	Lobar pneumonia	4-1	F	Lived
1934	W	33	iv	0	Toxemia, disproportion	C	0	0	0	G & E	Peritonitis	11-5½	F	Lived
1934	W	32	iv	2	Ruptured uterus 5 hr. before delivery	P	0	0	1 Rec.	G & E	Postoperative shock	6-8	F	Died
1934	P	26	ii	0	Membranes ruptured 5 days, attempted vaginal delivery	P	10¾ hr.	4 days	1 Vag.	G	Operative shock during manipulation			Dead
1935	W	44	xiv	0	Placenta previa	C	0	0	1 Vag.	E	Pneumonia on 5th P.O. day	7-5¾	F	Lived
1935	P	40	i	0	Disproportion, old primipara	C	0	0	0	G & E	Peritonitis	6-2	F	Lived
1935	P	29	i	0	Placenta previa; auto accident	B	3½ hr.	Yes	1 Vag.	G & E	Postoperative shock	6-12½	F	Lived
1935	P	29	ii	1	Disproportion and previous section	C	0	0	0	G & E	Pulmonary embolism on fourteenth day	7-10¾	M	Lived
1936	W	19	i	0	Severe T.B., tertiary syphilis	C	0	0	0	Local	Died in 5 days; T.B.	3-1½	M	Died in 9 hr.
1936	W	19	i	0	Contracted pelvis, disproportion	K	24½ hr.	16 hr. +	3 Rec.	G & E	Peritonitis	7-6½	M	Died 20 days after operation

1936	W	19	ii	1	Previous section, contracted pelvis, disproportion	G			0	G & E	Shock and hemorrhage on table	3-4	F	Lived 2 hr.
1936	W	30	iii	0	Fulminating eclampsia	G	0	0	0	Local	23 convulsions, died within 24 hr., eclampsia	3-12	F	Still-born
1936	W	41	iii	0	Twisted ovarian cyst	P	0	Artificially ruptured	1 Rec.	G & E	Peritonitis, died third P.O. day	7-5½	F	Lived
1937	W	21	i	0	Disproportion	K	27½ hr.	27	2 Rec. 3 Vag.	G & E	Postoperative shock in 4½ hr.	9-4	M	Lived
1937	W	34	iii	0	Post mortem in an attempt to save child; bronchopneumonia	PM G	0	0	0	None	Before operation	3-1	F	Still-born
Second Period														
1937	W	24	iii	0	Disproportion, previous C. S.	C	4 hr.	0	2 Rec. 1 Vag.	G & E	Shock during operation or anesthetic?	7-14½	M	Lived
1937	P	34	iv	0	Previous extensive plastic	C PM	0	0	0	Avertin	Avertin anesthesia death	9-12	M	Died
1938	W	38	iii	0	No advance in labor	P	20 hr.	0	4 Rec. 4 Vag.	E	Peritonitis on ninth day	10-2¼	M	Still-born
1938	W	31	iv	0	Placenta previa	G PM	0	0	1 Vag.	G & E	Respiratory failure before section was started		M	Still-born
1939	W	35	iv	0	Plastic and sterilization at 1 month	G	0	0	1 Rec.	G & E	Pneumonia	7-7¾	F	Lived
1939	W	24	iii	0	Previous C. S.	P	5 hr.	0	0	G & E	Shock during operation	7-4	M	Lived
1940	P	36	i	0	Cervical dystocia after 24 hr. labor	G	24 hr.	0	3 Rec. 2 Vag.	G & E	Intrapartum uterine bleeding	8-7	F	Lived
1941	P	23	i	0	Cervical dystocia	K	18¾ hr.	0	1 Rec. 2 Vag.	G & Vinethene	Cerebral embolism fourteenth P.O. day	8-3	M	Lived
1942	W	18	i	0	Premature separation	C		0	0	No + O_2	Shock during operation	7-7	M	Still-born

ence and capabilities of the individual will influence his judgment, and, if it is his judgment that cesarean section is the best method, preaching will not change it. The reputation of the individual is built on the soundness and acceptability of his judgment.

Anesthesia

In this report we have not tabulated the type of anesthesia. Generally the anesthetic was nitrous oxide plus oxygen through a closed mask supplemented with enough ether to avoid straining or asphyxiation of the patient. Within the last one and one-half years, open drop ether anesthesia following nitrous oxide and oxygen induction has been usually used.

The group at the Lying-in-Hospital believe that the routine anesthetic has not been ideal or quite satisfactory, and an effort to improve it has been made. Within the last nine months the prejudice against spinal anesthesia has been overcome, and it has been used on a number of patients, with very satisfactory results. The method used has been the fractional technique and as little as 75 mg. of novocain has been adequate with some patients, usually 150 mg. is the necessary dose. At times local novocain, avertin, or vinethene have been used as anesthetics; none of these have been used often enough to report on the results.

TABLE IX. RECORD OF INFANT MORTALITY

PERIOD	SINGLE BIRTHS	TWINS	TOTAL CHILDREN	STILLBIRTHS	NEONATAL PREMATURE	NEONATAL OTHER CAUSES	TOTAL	LIVING CHILDREN
7/1/32 to 7/1/42	1,310	12	1,334	30	49	34	113 or 9.2%	1,221
First period 7/1/32 to 7/1/37	657	8	673	19	30	20	69 or 10.25%	604
Second period 7/1/37 to 7/1/42	653	4	661	11	19	14	44 or 6.6%	617

Table IX shows the record of infant deaths for the whole period and for the first and second periods. There were 1,310 single births and 12 sets of twin births. Among these were 113 deaths, or an incidence of 9.2 per cent. Thirty of these infants were stillborn and 83 were neonatal deaths. Many of the neonatal deaths were among the prematures which were delivered by cesarean section because of placenta previa and premature separation of the placenta; it is obvious that the method of delivery had no bearing on the incidence of death among these infants. During the second period of this report, the infant death rate showed an incidence of 6.6 per cent which is about 40 per cent less than the infant death rate in the first period. This 6.6 per cent infant death rate is about twice the incidence of the infant deaths for all the babies delivered in the hospital for the last one and one-half years. This increased infant death rate cannot be attributed to the method of delivery, but could very often be ascribed to the complication which made the cesarean section necessary.

Discussion

This report has been submitted because it represents a rather large group of patients who have been delivered by cesarean section in a large

obstetric clinic by obstetricians and gynecologists of various training and capabilities. The report has been given in enough detail to determine what changes will be necessary in the management of some of our cases in the future.

The only divergence of this report from other comparable reports seems to be the incidence of the cesarean sections and the low proportion of the so-called low type operation. This is partly explained under Table IV but more explanation and discussion may be in order. Many men qualified to do obstetric and gynecologic surgery can do a low type operation with absolute confidence and safety. However, a large hospital staff is made up of individuals with various capabilities and experience. There are men on the staff who are especially capable to manage difficult vaginal deliveries and some of these men may not be especially interested or qualified in doing anything but simple surgery.

It is my belief that the low type cesarean section is a more difficult operation than the classical operation, and no one but an experienced obstetric surgeon should do them. An inexperienced surgeon subjects a patient to a greater danger in doing a low section than a classical operation on an elective case.

Summary

The tables and discussions have been given with an idea of showing the number, incidence, method, and results of 1,322 cesarean sections done in a large clinic during the past ten years.

Two five-year periods of work have been compared with the idea of seeing what changes occurred.

1. The report has demonstrated that the private service has increased during the second five-year period, and that the incidence of cesarean section has dropped on the private service.

2. The chief indications for cesarean sections have remained about the same.

3. The types of cesarean section have varied considerably but the tendency is toward the classical operation. There seems to have been no maternal mortality or morbidity which could be directly ascribed to the type of operation performed.

4. The maternal mortality rate was low for the 1,322 cases, an incidence of 1.96 per cent. During the second period of this report, it was 1.37 per cent for both private and ward services and during the second period of this report it was 0.65 per cent for 460 private patients.

5. The infant mortality rate was high during the first period of this report and showed considerable drop in the second period.

6. Finally, this report shows that the attitude toward cesarean section has changed some during two five-year periods, and that the results from the work have improved but still leaves something to attain.

I wish to thank Drs. Norris W. Vaux, Clifford B. Lull, Robert A. Kimbrough, and other members of the staff of the Philadelphia Lying-in-Pennsylvania Hospital for the privilege of using the records of their private patients which have been included in this report.

1806 SPRUCE STREET

Discussion

DR. LOUIS E. PHANEUF, BOSTON, MASS.—The study of 1,322 cesarean sections is of great value and may permit certain conclusions. Dr. Mohler mentioned the incidence which he feels is high, and yet, compared with that of other clinics, it might not be considered so.

The indications presented for cesarean section, in the main, were disproportion, previous cesarean section, placenta previa, and premature separation of the placenta. These correspond with the indications reported in other large series.

There are some differences of opinion in the employment of cesarean section in premature separation of the placenta which has been especially noticeable in the last decade. Many of these patients can be safely delivered through the pelvis, using cervical and vaginal tamponade after rupturing the membranes, applying a tight abdominal binder by means of a Spanish windlass or by other means. This causes more worry for the obstetrician during labor, but he may be recompensed by a quicker recovery of his patient. The decrease of cesarean sections in toxemia is in keeping with the present thought in obstetrics.

The paper draws attention to a decrease of the low cesarean section against the classical cesarean section during the last five-year period. The tendency in many clinics has been the opposite, that is, the increase has been in favor of the low cesarean section. The reasons given for the performance of the low cesarean section are twelve hours of labor, ruptured membranes and presumable infection. In this type of parturient, the low cesarean section certainly should be safer than the classical operation.

Other observers have made comparisons between the low and classical cesarean sections, and conclusions have been drawn that there is not much difference in their safety. To me the difference is marked. I am convinced of the increased safety of the low over the classical cesarean. If the low cesarean is safer for the individual who has had twelve hours of labor, ruptured membranes, etc., by the same token it should be safer for every woman who is subjected to an abdominal delivery.

The increased difficulties of the low operation are mentioned. It merely means the separation of the bladder, a simple procedure, and we have had no difficulty in teaching this method to residents.

Noteworthy in the paper is the lack of use of the extraperitoneal cesarean section which has increased the safety of abdominal delivery. The adoption of this method in my own work has reduced the incidence of cesarean-hysterectomy in the presence of presumable or existing infection. Formerly I did a number of Porro cesarean sections, having reported a series of 25 such operations without maternal mortality in 1931. With the advent of the extraperitoneal cesarean section, I have reserved cesarean-hysterectomy for women with uterine fibroids.

The death rate in this large series of cases reported by Dr. Mohler is not excessive. Unfortunately there will always be a death rate in cesarean section, the deaths frequently being due to the existing pathology for which the operation was performed, rather than to the operation itself. If a woman, with a certain pathologic lesion is delivered through the pelvis and dies, the death is usually ascribed to the pathologic lesion rather than to the method of delivery. On the other hand, if she is delivered by cesarean section, her death is ascribed to the operation. It is obvious that this method of reporting cases never results in favor of cesarean section.

The shock mentioned in connection with these patients can be overcome in most instances nowadays by the administration of blood plasma which is readily available. Although my experience with the use of the sulfa drugs is somewhat limited, I have found that they have reduced the morbidity to a considerable degree.

DR. IRVING W. POTTER, BUFFALO, N. Y.—Our series of cesarean sections covers something over 3,000 cases, but our maternal mortality is a little under 3

per cent for all types of cases. Now we have done practically no procedures but the so-called "high" operation. The rupture of the membranes after twelve hours of labor and vaginal examination have not had anything to do with our selection of type of operation. We feel that an operation that is above the navel is preferable because it is quicker; you can pack the uterus from above in potentially infected cases and can get the pack out in the first twenty-four hours and your patient does very well. In infected cases we would rather remove the uterus, and we do that before the removal of the baby which is an advantage in many ways. It is simpler, there is less loss of blood, and our patients do well. Altogether we have got along very well with confining our efforts to one type of operation.

DR. JAMES W. KENNEDY, PHILADELPHIA, Pa.—What I have to say in regard to cesarean sections in general, is in no way a criticism of Dr. Mohler's report. Cesarean section is the easiest operation to perform of all major abdominal surgery, and today it is too much enjoyed by an overenergetic profession. It is my opinion that over 95 per cent of cesarean sections performed tomorrow throughout the country could have been deliveries by the birth canal.

During my young and energetic days when I had charge of the Joseph Price obstetric course which was conducted in the slums of Philadelphia, I sent 50-odd patients to the Joseph Price Hospital for cesarean section. I was ordered by my old master to scrub my hands and deliver the supposed candidates for cesarean section. I did and but one patient had a cesarean section.

There is a postoperative history in cases of cesarean section which should be considered by every conscientious physician. To place a scar in the uterus and abdomen of a young woman during her first childbirth is to suspend a guillotine over her neck for the rest of her life. Where will she be during her next labor; will she fall in the hands of an accomplished surgeon, or will she die from a ruptured uterine scar?

We must have fewer cesarean sections and the mortality must approach that of normal labor in elective cases. We must also remember that every abdominal scar, as well as the uterine scar, carries a potential danger of postoperative bowel obstruction for the rest of the patient's life and the adage, once a cesarean always a cesarean, has weight. The obstetric woman is some one's patient from the cradle to the grave, and she is the greatest resource of the human race.

DR. J. BAY JACOBS, WASHINGTON, D. C.—I feel that the incidence of cesarean section as presented by the essayist is very high, particularly among private patients. Last year I reported about 740 cases that were classified as borderline, these representing one-twelfth of the total material. Cesarean section was performed in only 6 per cent of our borderline cases.

The fact that cesarean section is easy to do and so considered by a large group of obstetricians, is certainly no indication for its performance. It would be interesting to know in what proportion of patients operated upon for disproportion, x-ray pelvimetry had been used? Roentgenographic pelvimetry is recognized as one of the essentials preliminary to the performance of cesarean section in borderline cases.

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—I cannot forbear a word regarding deaths reported as from shock during operation, because we now have evidence that if there has been no excessive hemorrhage or traumatism during operation, such deaths are usually anesthetic deaths, due really to anoxemia, a common complication particularly since cyclopropane has been popularized.

A number of fatalities have occurred at the Philadelphia General Hospital which took place several days after the anesthetic was given. They would not have been recognized as anesthetic deaths had not the neuropathologist found the characteristic changes in prepared sections of the brain. McClure, using a selenium cell

over the web between the thumb and index finger, has demonstrated how common periods of anoxia not shown by the conventional signs are during anesthesia. Seven minutes' deprivation of oxygen is sufficient to cause the death of stellate cells and the cells of Purkinje. The operator should never permit a degree of cyanosis sufficient to darken the blood in the wound to continue.

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—I would like to know why in all of these studies of cesarean section there is such a definite distinction made between private and ward cases? It seems to me that they had better be put on the same basis. We do not divide carcinoma cases on this basis. Why should we make any distinction for cesarean sections?

DR. MOHLER (closing).—In reply to Dr. Kennedy's remarks, Fig. 1 shows the maternal deaths and the incidence of cesarean section in the Philadelphia area during a ten-year period. In 1931 there was about a 6 per cent maternal mortality

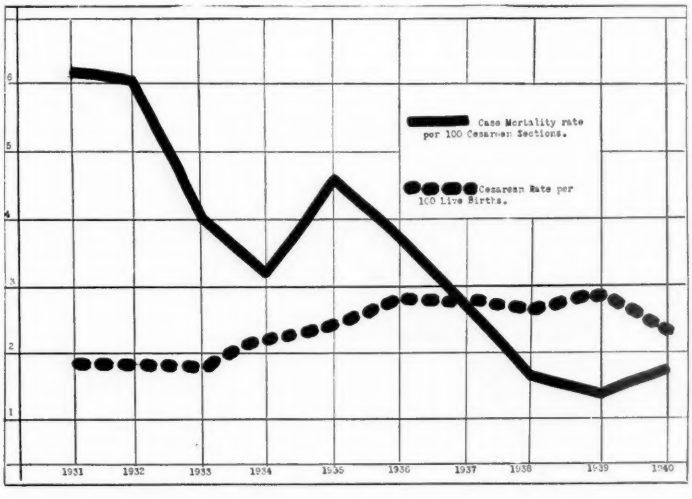

Fig. 1.—Cesarean section mortality in Philadelphia, 1931 to 1940. (Courtesy of Philadelphia Maternal Mortality Committee.)

from cesarean sections in the Philadelphia area. Since then the maternal mortality has dropped until in 1940 it was a little less than 2 per cent. The incidence of cesarean sections during the period of my report has increased almost 50 per cent in the Philadelphia area and during the same period the maternal mortality for cesarean sections has dropped two-thirds. It seems, therefore, that in spite of the fact that we are doing more cesarean sections, the incidence of maternal mortality has been lowered considerably.

In regard to Dr. Babcock's remark, some of the patients who supposedly died from shock were probably the victims of badly administered or wrongly selected anesthesia. I agree thoroughly with Dr. Babcock, and we have been trying to be more selective in our choice of anesthetic. Recently we have been doing a number of cesarean sections under spinal anesthesia with excellent results. We have not had enough experience to report but so far we are enthusiastic.

Dr. Kosmak has questioned the justifiability of reporting cesarean sections separately in reference to the ward and private services. The answer is evident in the report which shows the differences in the two services. The reason for this contrast cannot be a part of this report but should be studied.

URINARY INCONTINENCE IN WOMEN*

VIRGIL S. COUNSELLER, M.D., ROCHESTER, MINN.
(From the Division of Surgery, Mayo Clinic)

INCONTINENCE among women has been previously investigated by eminent physicians in all countries and various surgical procedures have been recommended for its correction. My intention here is, not to review all these methods, but to emphasize the importance of a careful analysis of the cause of the incontinence and also to emphasize that a complete understanding of the anatomy of the vesical neck, urethra, and pelvic fascia plus the normal physiology of micturition is imperative before one undertakes any surgical corrective procedure. It seems to me that the very careful experimental work on this subject by Kennedy[4] has done more to clarify it than any previous contribution and I wish to elaborate and emphasize some of his suggestions because of their accuracy and fundamental importance.

Incontinence may either be congenital or acquired. In the former group it is caused by a congenital defect, the extreme of which is represented by exstrophy of the bladder. Partial epispadias usually is the most confusing because in some instances, objectively at least, the anatomic relations appear normal but on cystoscopic examination the musculature of the dorsal portion of the urethra is missing. There may be faulty development of the pelvic fascia which supports the bladder and of the musculature of the vesical neck and urethra. In spite of this, the urethra may function normally for many years, but when some atrophy develops during the menopause, various degrees of incontinence follow. One other congenital defect which must be mentioned in this connection is spina bifida. The defect of innervation may not be sufficient to produce incontinence until after a normal delivery. Here the anatomic relations of the vesical neck and urethra are undisturbed, and unless the defect is recognized surgical correction to the urethra and vesical neck will fail. Furthermore, it must be recognized that slight trauma of any type may initiate incontinence when spina bifida exists.

Acquired incontinence, in which we are primarily interested, is that seen incident to childbirth and less commonly that incident to operations for cystocele and prolapse. The incontinence may vary from moderate to severe, depending on the degree of trauma. Not all of these patients require cystoscopic examination, but a direct query regarding leakage of urine, when vaginal plastic procedures or vaginal hysterectomy is contemplated, is essential. Some patients who have complete procidentia do not have any incontinence while others who have very slight

*Read at the Fifty-Fifth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 10 to 12, 1942.

cystocele or urethrocele may have severe incontinence, which perhaps is the major complaint for which they seek treatment. Cystoscopic examination in cases of severe incontinence will reveal whether the urethra is distorted or the internal sphincter is gaping or fixed.

Fig. 1.—Female urethra located behind symphysis and embedded in anterior vaginal wall.

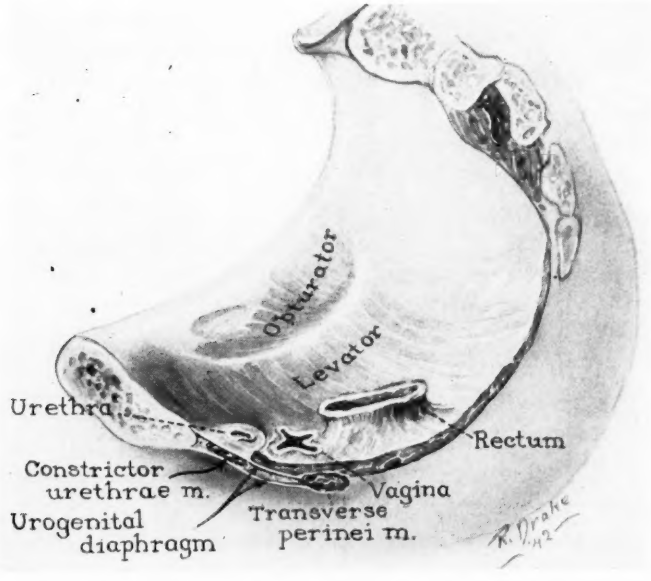

Fig. 2.—Relation of the muscles of the urethra and urogenital diaphragm (sagittal section).

Anatomy of Vesical Neck and Urethra

The female urethra measures 4 to 4.5 cm. in length. Both the urinary bladder and the urethra are surrounded by loose areolar tissue which

is an extension of the pelvic fascia. This tissue becomes firm and fixed at certain points for protection and support, as at the vesicouterine reflection, at the ureterovesical junction and the entire ventral surface of the urethra. The urethra is further fixed and suspended in its normal position to the pubis by the pubovesical ligament. According to Gray "the female urethra is placed behind the symphysis pubis, imbedded in the anterior wall of the vagina, and its direction is obliquely downward

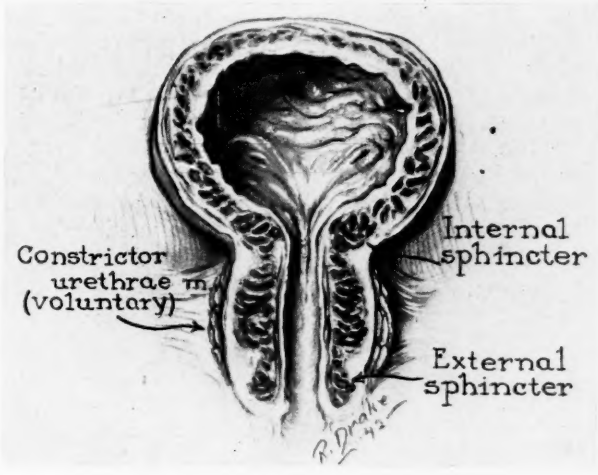

Fig. 3.—Musculature of the urethra.

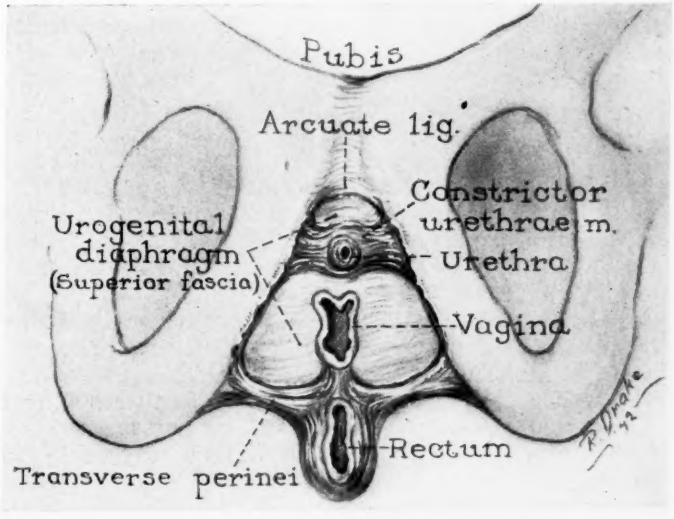

Fig. 4.—Diagrammatic view of constrictor urethrae muscle and urogenital diaphragm.

and forward; it is slightly curved with the concavity directed forward [Fig. 1]. It perforates the fasciae of the urogenital diaphragm, and its external orifice is situated directly in front of the vaginal opening."

The principal muscular coat is circular and is continuous with that of the bladder. Over the posterior third of the urethra and the neck

of the bladder this circular muscle is thickened and is called the internal urethral sphincter or sphincter vesicae. This circular muscle thins out over the outer third of the urethra and over the remaining portion of the bladder. It also, by a slight thickening at the external meatus, gives rise to what has been designated as the external involuntary urethral sphincter. There are a few inner longitudinal smooth muscle fibers (Fig. 2). These two urethral sphincters are involuntary, which is exactly the same as a smooth muscle sphincter of circular fibers anywhere else in the body. In more recent editions of *Gray's Anatomy* a striated voluntary sphincter is described. It lies between the superior and the inferior layer of the urogenital diaphragm, covering the middle and posterior thirds of the urethra (Fig. 3). It is designated the sphincter urethrae membranaceae. Its external fibers arise from the junction of the inferior rami of the pubis and ischium to the extent of 1.25 to 2 cm. and from the neighboring fasciae. They arch across the front of the urethra and bulbourethral glands, pass around the urethra and behind it, and unite with the muscle of the opposite side by means of a tendinous raphe (Fig. 4).

Innervation of the Sphincters*

The innervation of the internal vesical sphincter is still the subject of much controversy and its exact innervation has not been completely established. Until recently it was believed that there was a dual innervation of the bladder and vesical neck through the sympathetic and parasympathetic divisions of the autonomic nervous system. The former was thought to cause contraction of the internal vesical sphincter and relaxation of the detrusor and was, therefore, known as the "nerves of filling" while the latter, or parasympathetic innervation, was known as the "nerves of emptying" since it was known to cause contraction of the detrusor and relaxation of the internal vesical sphincter. Evans has seriously questioned this hypothesis recently and has presented evidence which strongly suggests that the innervation of the internal vesical sphincter is solely through the parasympathetic system. Denny-Brown and Robertson expressed the same point of view and showed that the internal vesical sphincter serves a reciprocal relation with vesical contraction, its opening depending on vesical contraction and its closure on the subsidence of vesical contraction. The function of the internal sphincter is, therefore, reflex and is not immediately under voluntary control.

Mention has not been made of the sphincter trigonalis, thought to be innervated by the sympathetic nervous system, since its role in the opening and closure of the internal vesical orifice has not been too well established. The problem is complicated still further by the fact that McCrea has found striated muscle fibers among the smooth muscle fibers of the internal sphincter, and this, if true, may be of great functional significance.

The innervation of the external urethral sphincter or compressor urethrae is through the somatic nervous system via the pudic or internal pudendal nerves and its function is to defer or postpone micturition. Denny-Brown and Robertson have presented evidence that suggests that this sphincter can be voluntarily contracted but not voluntarily relaxed. Its relaxation is apparently reflex and depends on vesical contraction

*I am indebted to Dr. C. E. Jacobson for the portion of this paper on innervation of the sphincters.

or relaxation of the internal sphincter. Learmonth has shown that the external urethral sphincter among women is not indispensable as he has sectioned both pudic nerves and did not note any incontinence.

While the levator ani, deep perineal and bulbocavernosus muscles can hardly be considered as true sphincters they are nonetheless often spoken of as "accessory sphincter muscles" and their co-ordinated contraction or relaxation as "associated movements." Denny-Brown and Robertson stated that there is little doubt that the levator ani and perineal muscles are relaxed during micturition and that they may be thought of as having accessory sphincter control.

Comment

The first concrete evidence of this voluntary sphincter function was demonstrated by Kennedy[4] in 1937, using a urethral bag and measuring the amount of pressure in centimeters of water which was required to overcome the sphincteric action of the internal urethral sphincter and the sphincter membranaceae under normal conditions. The information ascertained by this method, which is of extreme importance, is that the sphincter around the middle third of the urethra resisted twice as much pressure as did the internal third of the urethra. This method was then used as a diagnostic procedure for women who had incontinence and without exception the relative weakness of the membranous portion of the urethra could be demonstrated. Continence was similarly demonstrated following reconstruction of the muscular support of the middle and inner portions of the urethra. Kennedy[5] concluded that there is an involuntary sphincter muscle about each of the inner and outer thirds of the urethra and that there is an additional sphincter about the middle third which is probably under voluntary control.

There is other direct evidence which confirms Kennedy's findings. For example, internal sphincterotomy can be performed on a woman without causing incontinence. Also, by using a panendoscope to examine the urethra and bladder, the middle third of the urethra can be seen to contract and relax voluntarily as suggested to the patient. Resection of the vesical neck and inner third of the urethra without producing incontinence would seem to me to be sufficient proof that the internal vesical sphincter is of less importance than the sphincter over the middle third. This was actually done by my colleague (Priestley) on a patient sixty years of age for carcinoma of the bladder involving the vesical sphincter. The entire sphincter and the first centimeter of the urethra were resected and the stump of the urethra was anastomosed to the bladder at the apex of the trigone. The patient remained continent up until a few weeks before her death which was due to recurrence. The final period of partial incontinence was most likely the result of local recurrence.

It is now quite clear that the sphincter mechanism of the female urethra is more delicate and complicated than previously considered. When we regarded the urethra as having an internal and an external

urethral involuntary sphincter connected by an epithelial lined tube 4 cm. in length, the incontinence was thought to be the result of damage to the internal vesical sphincter only. This may be true still in certain mild instances of incontinence but in most cases the damage extends beyond this sphincter and involves the voluntary sphincter also, which, according to Gray, surrounds the entire membranous urethra and, therefore, it covers the internal sphincter, or as Kennedy[5] states, it reinforces the internal sphincter.

The sphincter urethrae membranaceae is exactly the same in men with this one exception, that the prostate is interposed between it and the internal vesical sphincter. In men it is designated as the cut-off muscle or the external urethral sphincter. From this arrangement it is clear why incontinence does not occur when internal sphincterotomy, transurethral resection of the prostate, or complete enucleation of the prostate is performed, unless the sphincter urethrae membranaceae is injured. Urologists, therefore, treat this sphincter muscle with extreme care and I am certain that its homologue in women deserves the same care and attention. The surgical approach in women is much simpler than in men and the technique of exposure and repair is not complicated.

Kennedy[6] has stressed the method of injury to the sphincter mechanism that occurs during childbirth and it should be emphasized. Trauma during delivery is between the urethra and the symphysis or the inferior rami of the pubis from prolonged pressure. The internal sphincter is forcibly stretched and the voluntary sphincter is separated from its medial ventral attachment on the urethra. Distortion of the urethra or fixation of any portion of the sphincter mechanism to the pubic rami he regards as a very definite cause of incontinence. Distortion or fixation is brought about most likely from hemorrhages into the muscle and along the urethral shaft, which finally result in adhesions with shortening and fixation of the sphincter mechanism to the pubis or rami. Such deformities he has demonstrated by roentgenograms of the urethra in patients prior to surgical repair and in patients who were unimproved or made worse by surgical repair using the Kelly method.

Incontinence which comes on following a repair for cystocele, or vaginal hysterectomy for prolapse that did not exist prior to operation is very disappointing to both patient and surgeon. The sphincter mechanism was intact even though the anterior vaginal wall was down, but when the repair of the cystocele was executed the voluntary sphincter support was not replaced after being separated from the vaginal wall. This complication can be avoided if the possibility of surgically producing incontinence while repairing a cystocele or performing vaginal hysterectomy is kept in mind.

The Kennedy Operation

The cervix is grasped with a tenaculum and the anterior vaginal wall opened in the usual manner to within 1.5 cm. of the external urinary

meatus (Fig. 5). The urethra is separated from the pubic rami on each side. This separation must be kept close to the bone to avoid a plexus of veins and branches of the inferior vesical artery, and must extend into the paravesical space. If this is gently done, fibrous adhesions between the urethra and pubic rami can be palpated and separated, restoring freedom of motion to the urethra. This freedom of motion must be maintained for complete relief of incontinence. This is accomplished by plicating the tissues under the urethra by three mattress sutures which hold the urethra from the pubic rami (Fig. 6). A second row of

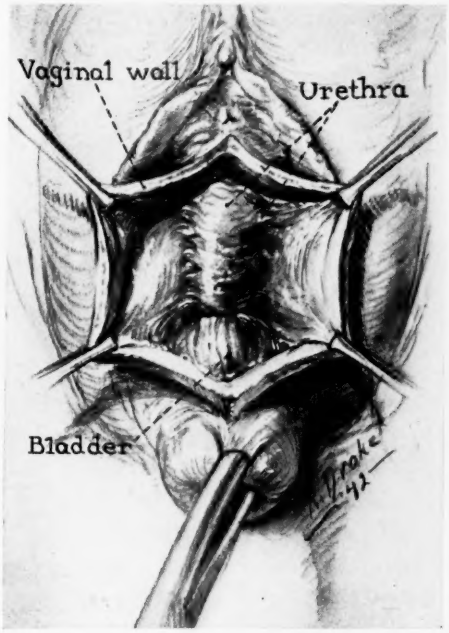

Fig. 5.—Anterior vaginal wall opened to 1.5 cm. of external urethral meatus.

mattress sutures picks up the edges of a fascia-like structure on the lateral surface of the urethra and these sutures when tied separate the urethra further from the pubic rami (Fig. 7). An additional mattress suture should be placed to plicate the inner portion of the urethra about the internal sphincter (Kelly stitch).

The restoration of the voluntary sphincter is now to be considered. The damaged portion of this muscle which remained attached to the vaginal wall is removed with the redundant portion of the vaginal wall which formed the urethrocele. The remaining intact sphincter fibers are replaced by three No. 1 chromic catgut sutures beginning at the highest point of the vestibule and extending down about 2 cm. These sutures are passed through the vaginal wall quite close to the pubic rami so as to be certain to catch the muscle fibers of the constrictor urethrae (voluntary) and inferior layer of fascia of the urogenital diaphragm. When these are tied the edges are replaced beneath the middle and inner portions of the urethra (Fig. 8). Kennedy[7] uses silver wires instead of catgut. A male catheter is placed in the urethra for five to seven days or until the patient is out of bed, when she is advised to void as normally.

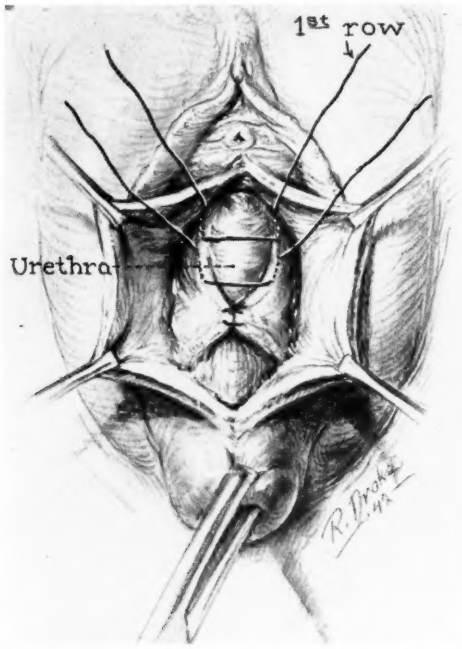

Fig. 6.—First row of mattress sutures plicating urethra.

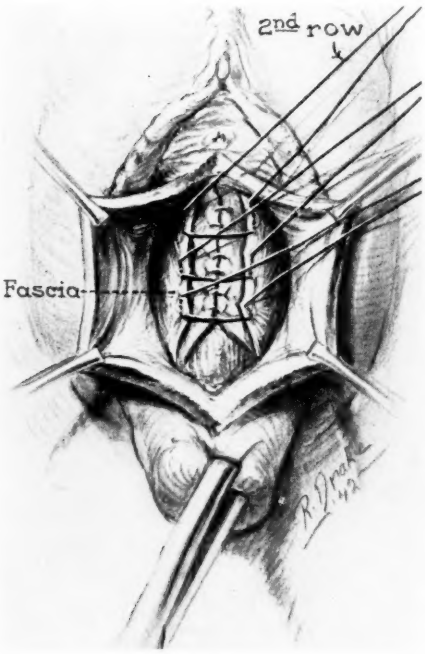

Fig. 7.

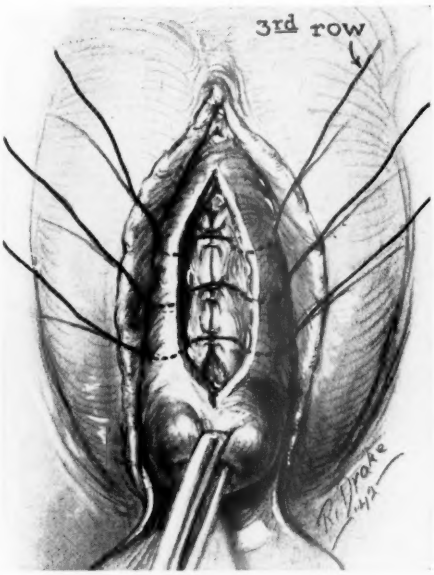

Fig. 8.

Fig. 7.—Further separation of urethra from pubic rami by second row of mattress sutures.

Fig. 8.—Reconstructing constrictor urethrae muscle and urogenital diaphragm beneath the urethra.

Results

The author has performed the Kennedy operation on 26 patients either as a primary procedure for various degrees of incontinence or in association with other surgical procedures for cystocele, prolapse, small fibroids, menometrorrhagia and lacerated perineum. The result in every instance was complete restoration of continence. Some patients contracted cystitis and urethritis of varying degrees, which induced some urinary urgency and frequency. These symptoms were all relieved through treatment in the Section on Urology before the patients were dismissed (Table I).

TABLE I. KENNEDY OPERATION

Complete Urinary Continence Restored in All 26 Patients in Whom the Procedure Was Carried Out by Author*

CASE	AGE, YEARS	SURGICAL DIAGNOSES			ASSOCIATED OPERATIONS‡
		INCONTINENCE, GRADE†	CYSTOCELE, GRADE†	OTHER CONDITIONS	
1	49	1+	2		Vaginal hysterectomy
2	37	1	1		
3	40	2			
4	49	2	2	Prolapse, Grade 2	Vaginal hysterectomy
5	51	3			
6	44	2+			
7	52	2	2	Prolapse, Grade 1	Vaginal hysterectomy
8	40	3			
9	42	2	2	Prolapse, Grade 1	Vaginal hysterectomy
10	54	1+		Prolapse, Grade 4	Vaginal hysterectomy
11	42	1+		Fibroids	Vaginal hysterectomy
12	53	2	3	Prolapse, Grade 2	Vaginal hysterectomy
13	43	2	3		Vaginal hysterectomy
14	65	2			
15	48	1+	3	Prolapse, Grade 2	Vaginal hysterectomy
16	48	1+			
17	36	2+			
18	47	2+			
19	53	2	2+	Fibroids	Vaginal hysterectomy
20	67	1	2	Prolapse, Grade 2	Vaginal hysterectomy
21	44	3			
22	54	2+	3	Fibroids	Vaginal hysterectomy
23	51	1+		Menometrorrhagia	Vaginal hysterectomy
24	39	1+	1	Fibroids	Vaginal hysterectomy
25	51	1	1+		
26	49	2		Menometrorrhagia	Vaginal hysterectomy

*These results should be contrasted with other methods which showed 35 per cent failures.

†On a basis of 1 to 4, in which 1 designates the mildest and 4 the most severe condition.

‡Perineum was repaired wherever indicated.

Conclusions

The female urethra has an internal urethral and an external involuntary urethral sphincter. In addition there is a voluntary sphincter surrounding the middle third and extending posteriorly to cover the internal urethral sphincter partially. This sphincter is designated the sphincter urethrae membranaceae (Gray) and is the same as the external urethral sphincter in the male. Kennedy's[7] investigation of this sphincter mechanism has served to clarify the real cause of incontinence

and he suggested a method of repair which has greatly improved the results.

It is hardly fair to state that this operation should be performed in every instance of incontinence, since records show that 60 to 75 per cent of patients received good results by other methods. The high percentage of failures when other methods were used should represent that group of patients who exhibit more damage to the sphincter mechanism than relaxation of the internal sphincter and proximal centimeter of the urethra. The author has used the method of repair suggested by Kennedy for 26 patients, all of whom were completely relieved of their incontinence.

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Discussion

DR. BAYARD CARTER, Durham, N. C.—My experience is limited to 8 cases. Operation was found necessary in 5 cases following a vaginal operation, in 1 following a cystocele and in 2 virgins who developed incontinence late in life. The difficulties we have had in the procedure are first to satisfy ourselves that we have been able to free the urethra and then to control the bleeding. In the old days we thought that 65 per cent of the cases would have good results with the ordinary Kelly procedure, but we do not feel so today and therefore incorporate the tension on the urethra in operations for true procidentia. We also use it in those cases of vaginal hysterectomy that develop incontinence of urine. It also makes an ideal conservative procedure in the occasional case of an aged virgin who develops an incontinence, either with or without an hypertrophied cervix.

DR. A. J. RONGY, New York, N. Y.—A word should be said about prevention in connection with urinary incontinence. Those of us who have had extensive obstetric experience have observed that the patients who have a thick, bony pubis and a low pubic arch, are more prone to develop incontinence in later life than those who have a high and normal pubic arch. Therefore such patients should not be allowed to have a prolonged second stage of labor because of the greater likelihood of damage to the anterior vaginal wall, including the neck of the bladder and the urethra.

Incontinence in virgins occasionally may be observed as a result of masturbation. I recollect an incident of this kind in a woman who admitted to excessive masturbation and frequently complained of urinary incontinence. She had no pathologic lesions to account for it.

DR. A. D. CAMPBELL, Montreal, Canada.—The compressor urethrae muscle, lying between the layers of the so-called urogenital diaphragm, is in reality the deep perineal muscle but only a portion of this muscle (the anterior portion) is compressor in effect. One therefore cannot expect the compressor urethrae muscle to function properly when the free margin of the urogenital diaphragm is lacerated, for it is in

this fascia that the compressor urethrae muscle is actually fixed. Hence in reconstructing the muscular support of the urethra one must not overlook the remaining portion of the urogenital diaphragm.

I am of the impression that in a great proportion of cases previously operated upon for damaged birth canal the abdomen has been opened as part of the surgical procedure. The subsequent frequency in such cases is not due to the improper support of the urethra but to the adhesions of the bladder to gut, adnexa or omentum. The factor of extravesicular adhesions must always be considered.

DR. COUNSELLER (closing).—Dr. Carter stressed the question of bleeding during separation of the urethra and bladder from the pubic rami, and that is a very important point. If the inferior vesical artery is injured there will be considerable bleeding, and sometimes it cannot be avoided. I try to separate the bladder from the rami by keeping outside of the vascular plexus and adjacent to the bone. It may be impossible to control bleeding by ligature or suture. In such instances I simply put in a piece of iodoform gauze, and leave it in position for from three to five days.

It is also important that in the process of reconstruction the urethra be straightened. That is one of the primary purposes of the operation; another one is that of lengthening the urethra. Many times it is foreshortened, as beautifully illustrated in Dr. Kennedy's work.

I think what Dr. Campbell has said concerning scarring resulting from previous surgical treatment is particularly true if during abdominal hysterectomy an attempt was made to reconstruct the uteropubic fascia. If such procedures have not been done, much difficulty will not be encountered in reconstructing muscular control from the vaginal side, as in the Kennedy operation.

POSTERIOR VAGINAL ENTEROCELE*

Hernia of the Cul-de-sac of Douglas

LOUIS E. PHANEUF, M.D., SC.D., F.A.C.S., BOSTON, MASS.
(From the Carney Hospital)

POSTERIOR vaginal enterocele, or hernia of the cul-de-sac of Douglas, is a lesion which up to two decades ago had received but little attention in the literature. That it is fairly common is attested by the number of publications appearing during the last twenty years. In 1924, at the Cleveland meeting of this Association, I[1] presented a paper on this subject, reporting 4 personal cases. Since then my series has reached the number of 48, the results in which are reported below.

In 1909, Marion,[2] of Paris, brought this condition to the attention of the profession and described an abdominal method of obliterating the cul-de-sac of Douglas. In 1912, Moschcowitz[3] described a similar procedure for the cure of prolapse of the rectum, this being equally applicable to hernias of the cul-de-sac of Douglas. In 1922, George Gray Ward[4] discussed the subject of posterior vaginal enterocele before the American Medical Association and described a vaginal operation to overcome this condition.

Previous to the publication of these papers, posterior vaginal enteroceles were described, as they still frequently are, as high rectoceles. That this is fallacious may be proved by a careful dissection of the posterior vaginal segment, where there will be encountered a bulging of the cul-de-sac of Douglas above the rectum, the two being separated by a layer of adipose areolar tissue. The upper limit of the rectum may be demonstrated by introducing into it a well-lubricated gauze sponge at the end of a sponge stick or a ring forceps, when the mass bulging over the rectum will be found to be the cul-de-sac of Douglas. The contents of the mass may consist of large or small intestines, or omentum, or all three.

There are two etiologic factors responsible for these hernias: first, an abnormally deep cul-de-sac of Douglas, a congenital defect. With intra-abdominal pressure directed against the cul-de-sac, traction is made on the posterior lip of the cervix and on the anterior wall of the rectum, resulting in prolapse of the uterus, the rectum, and the anteriorly attached bladder. By this mechanism, a congenitally deep cul-de-sac of Douglas may be responsible, in most cases, for the so-called nulliparous prolapse. A second factor rests in the trauma of labor, consisting in the

*Read at the Fifty-Fifth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 10 to 12, 1942.

tearing or stretching of the thin rectovaginal fascia during parturition, and especially during operative deliveries; this results in the formation of a hernial sac, which keeps increasing in size as time goes on.

A hernia of the cul-de-sac may follow vaginal hysterectomy for the treatment of prolapse, if the cul-de-sac is not closed or obliterated. This may be prevented by approximating the uterosacral ligaments to each other in their entire length, as a part of the technique in all vaginal hysterectomies for the treatment of prolapse, since the united ligaments will act as a definite barrier against recurrence. Posterior vaginal hernia may also occur following a commonly accepted method of treating prolapse, namely amputation of the cervix, anterior colporrhaphy, perineorrhaphy, and fixation of the uterus to, or its incorporation in, the abdominal wall. Following this intervention a wide space is left posteriorly between the cervix and the rectum. In the course of ten to fifteen years, by my observation, a large hernia of the cul-de-sac of Douglas may develop. I have operated upon several women with such a recurrence.

There are three accepted methods of surgically treating these hernias: the abdominal method, recommended by Marion and Moschcowitz; the vaginal, proposed by George Gray Ward; and finally colpocleisis, total or subtotal. The Ward vaginal operation is the ideal method, the abdominal being reserved for the very large and complicated hernias with adhesions, which make the vaginal dissection very tedious, if not hazardous. Colpocleisis is employed in large hernias, where there exist contraindications to a laparotomy.

The vaginal intervention consists in freely dissecting the posterior vaginal segment to the cervix uteri or the vaginal vault, exposing the rectum and cul-de-sac hernia, picking the cul-de-sac, freeing it from all surrounding structures, opening it, reducing its contents, ligating its base, and resecting it. The uterosacral ligaments are then approximated in their entire length by interrupted sutures of fine silk or catgut, and the pelvic floor is repaired. The abdominal procedure relies upon the application of superimposed purse-string sutures, from below upward, in order to obliterate the cul-de-sac, using due care not to include the ureters in these sutures. If one is in doubt about the course of the ureters, catheters may be introduced into them as a preliminary step.

TABLE I. AGES

	PATIENTS
Between 35 and 40 years	5
Between 40 and 45 years	8
Between 45 and 50 years	4
Between 50 and 55 years	10
Between 55 and 60 years	8
Between 60 and 65 years	9
Between 65 and 70 years	3
Between 70 and 75 years	1
	48

The youngest patient was 36, and the oldest 73 years of age.

TABLE II. DIAGNOSES

Posterior vaginal enterocele (Hernia of cul-de-sac of Douglas)	48
Additional Diagnoses	
Uterine procidentia	9
First-degree prolapse	1
Recurrent prolapse	3
Virginal prolapse	3
Prolapse of cervical stump	2
Hypertrophied cervix	2
Ulcer of cervix	1
Laceration of cervix	2
Cervical polyps	2
Cystocele	7
Rectocele	10
Vaginal ulcer	2
Hypertrophied suburethral fold	1
Complete laceration of perineum	1
Prolapse of rectum	1
Ventral hernia	2
Myomas of uterus	2
Diabetes	1
Cholelithiasis	1

TABLE III. PREVIOUS OPERATIONS FOR PROLAPSE IN THIS GROUP

OPERATIONS	PATIENTS
One previous	17
Two previous	4
Three previous	4
	25

25 of the 48 patients had had previous operations for prolapse.

TABLE IV. OPERATIVE PROCEDURES

Ward vaginal operation	36
Moschcowitz operation	10
Total colpocleisis	1
Partial colpocleisis	1
	48
Additional Operative Procedures	
Vaginal hysterectomy	6
Interposition operation	6
Supravaginal hysterectomy	4
Fundectomy	1
Abdominal fixation of uterus	4
Incorporation of uterus in abdominal wall	1
Cervicopexy (abdominal)	4
Amputation of cervix	6
Trachelectomy (cervical stump)	1
Cauterization of cervix	1
Anterior colporrhaphy	1
Colpoperineorrhaphy	38
Bladder advancement	1
Resection of suburethral fold	1
Myorrhaphy of sphincter ani	1
Double salpingo-oophorectomy	4
Appendectomy	1
Cholecystectomy (2 weeks after plastic operation)	1
Incisional herniotomy	2
Hemorrhoidectomy	1

TABLE V. ANESTHESIA

	PATIENTS
Spinal anesthesia	20
General anesthesia	28
	48

TABLE VI. MORTALITY

There was one death in 48 patients, a mortality of 2.08 per cent.

This patient, 73 years of age, was operated upon under spinal anesthesia, 100 mg. of novocain crystals having been used. The intervention consisted of an interposition operation, vaginal resection of the cul-de-sac of Douglas, approximation of the uterosacral ligaments and colpoperineorrhaphy.

The operation was performed on May 15, 1928. On May 16, 1928, she had a small pulmonary embolus, from which she recovered. On May 22, 1928, one week after operation, she had a second massive pulmonary embolus which took her life.

TABLE VII. RESULTS

There were three recurrences, Cases 2, 5, 19, 6.2 per cent

Case 2: Recurrence after Moschcowitz operation; six years after recurrence, total colpocleisis was performed, with a satisfactory result.

Case 5: Slight bulging of cul-de-sac after the vaginal operation.

Case 19: Slight bulging of cul-de-sac after the vaginal operation.

Results

The follow-up in this group of elderly patients, recruited from the New England States, has not been entirely satisfactory, as it has been difficult to bring them in for subsequent examination. All were examined at the time of their discharge from the hospital, and showed satisfactory primary results. They were re-examined within a year of operation, and 3 recurrences were discovered. Several of the oldest patients died of intercurrent disease. It must be borne in mind that in checking the results of vaginal hernias of any type, the more years are allowed to elapse, the higher will be the percentage of recurrences. Were we able to examine all of the patients alive at this time, our recurrences would probably be higher than 6 per cent. These operations were performed during a period of twenty years.

Summary and Conclusions

1. A deep cul-de-sac of Douglas may be congenital or be acquired as the result of parturition. In either case it plays an important role as a cause of uterine prolapse.

2. A hernia of the cul-de-sac may occur after a vaginal hysterectomy for prolapse if care has not been taken to approximate the uterosacral ligaments in their entire length at the time of operation.

3. A large hernia may develop following the combined method of operating for uterine prolapse, namely amputation of the cervix, anterior colporrhaphy, perineorrhaphy, and fixation of the uterus to, or its incorporation in, the anterior abdominal wall. Following this operation a

wide space is left between the cervix and the rectum, through which a hernia may develop in the course of years.

4. A hernia of the cul-de-sac of Douglas should be differentiated from a high rectocele.

5. Lack of recognition of this condition leads to failures in operations on the posterior vaginal segment.

6. Vaginal and abdominal operations have been devised for the correction of this lesion.

7. The vaginal route is employed in most cases, while the abdominal route is reserved for very large hernias, and those complicated with adhesions.

8. Forty-eight cases of posterior vaginal enterocele are reported.

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Discussion

DR. A. D. CAMPBELL, Montreal, Canada.—In looking over our statistics in the Gynecological Clinic of the Montreal General Hospital, over a five-year period, it was found that an enterocele was present in some 4.5 per cent of cases referred to us for repair of a damaged birth canal.

In the diagnosis, particularly in its smaller forms, an enterocele is often overlooked, particularly if it coexists with a rectocele. With the patient in the lithotomy position vaginal enterocele, or so-called high rectocele, becomes very much less apparent or may even seem to disappear. It is furthermore a problem to decide whether or not one is justified in repairing the smaller forms of this condition when the patient presents no symptoms which one can ascribe to the enterocele.

While it is true that with a sponge on a ring forceps, as described by Dr. Phaneuf, one can usually demonstrate the presence of an enterocele, there are cases in which one cannot be sure even by such a method. If there is any doubt as to the presence of an enterocele a small incision should be made through the vaginal vault as a preliminary to repair. Through this opening the cul-de-sac can be thoroughly explored and if a hernia exists its lower limit can be determined with accuracy. I have found that such a procedure is infinitely more informative and one less likely to damage the anterior wall of the rectum than any attempt to demonstrate or isolate the hernial sac by dissection.

In the repair of enterocele I am thoroughly in accord with Dr. Phaneuf that vaginal hysterectomy gives the most satisfactory surgical approach. By removal of the uterus all the structures concerned in this condition are more accessible to repair and can be more effectively employed to occlude the hernia. After the hernial sac is completely closed with a purse string suture and the excess peritoneal sac resected, the uterosacral ligament can be easily sutured into the pubocervical fascia and approximated to reduce the hiatus anterior to the rectum. In the repair of the posterior vaginal wall following the surgical resection of the vaginal hernia, the rectovaginal septum and the so-called urogenital diaphragm should be meticulously reconstructed so as to insure adequate support to the rectum and its ampulla.

Unfortunately, there are self-styled gynecologists who still think that procidentia or an enterocele or a damaged birth canal can be permanently corrected by affixing

the uterus to the anterior abdominal wall. Such fixation in addition to being a futile operation, rather complicates subsequent vaginal herniotomy with vaginal hysterectomy as an incident in the procedure. The fixation pedicle in such cases is an object which has to be dealt with. Fortunately it can be ligated easily by passing a ligature around its stock. With the assistance of an ordinary bifid packing probe the knot can be slid upwards to its base and tied tightly so as to prevent oozing.

DR. JAMES W. KENNEDY, PHILADELPHIA, PA.—I have never liked the term "enterocele," as it suggests that the intestine has been a factor in its production which I do not believe is true. In several thousand vaginal hysterectomies where we have freely incised the posterior vaginal vault, entering the cul-de-sac of Douglas, I have never found the intestine in the cul-de-sac. The intestine does not prolapse until air has entered the pelvis.

If the fascia of the vaginal fornix and the uterosacral ligaments both are atrophied and lose their function, a true enterocele will not be found, but if the fascia of the vaginal fornix alone gives way and the uterosacral ligaments are intact, then the true enterocele makes its appearance and gives the posterior vaginal wall the dumbbell appearance.

In nearly all the patients I have seen, there has been a marked degree of prolapse of the uterus with a marked cystocele and so I perform vaginal hysterectomy by the clamp method. The ideal procedure in these cases of late prolapse where enterocele and rectocele become a common lesion from descent of the uterus, is first to perform a vaginal hysterectomy by the clamp method combined with a radical cystocele operation, and later to do a high posterior repair of the vaginal wall. The retraction of the vaginal fornix incidental to the clamp method of vaginal hysterectomy and the extensive cystocele operation, followed later by a high repair of the posterior vaginal wall, has always given perfect relief of the miserable condition.

Substantial suture material must be used and we employ silkworm-gut in all our repairs.

DR. WILLIAM H. VOGT, ST. LOUIS, MO.—I am not very often able to make the diagnosis of enterocele before the operation is started. The diagnostic method that Dr. Phaneuf has brought out, namely by putting a sponge into the rectum, applies after the operative field is exposed. Even then it may be difficult and not until you have dissected the tissues thoroughly do you recognize that you are dealing with an enterocele. In some cases even we have believed that we had done a nice repair of a rectocele but the patient has returned with a bulging over the perineum bigger than it was before the operation. In such cases we have failed to recognize the condition.

I was glad to hear Dr. Phaneuf admit that if you watch these patients long enough you will see a number of recurrences, even though you have done the enterocele operation carefully, because after a number of years some patients, who are obliged to do hard work, or who inadvertently lift heavy objects, have a recurrent enterocele or a prolapse after the original operation.

I would like to ask Dr. Phaneuf how he would handle a prolapse of the posterior vaginal wall, which proved to be an enterocele, in a patient in whom a vaginal hysterectomy had been done and who is still in the years of sexual activity, not much over 40 or 45 years old? Should another attempt be made to dissect out the hernial sac and close it in the same manner as in the original operation?

DR. BENDER Z. CASHMAN, PITTSBURGH, PA.—Unrecognized enterocele, is, I believe, the most common cause of recurrence after prolapse of the uterus. The new lesion, however, is not always an actual recurrence of the prolapse of the uterus itself. The cervix or vault of the vagina after these operations may be held rather

high, while the prolapsed area is posterior to the cervix and is due to enterocele. This is a true hernia. You can feel the small intestines and some of them are huge. I feel, with Dr. Phaneuf, that in such a condition after the uterus has been entirely removed the most satisfactory procedure is colpectomy.

DR. LEWIS F. SMEAD, TOLEDO, OHIO.—One of the most common failures in an operation for prolapse follows the Mayo type of operation in which the broad ligaments are brought together and fastened well forward under the symphysis. This leaves a weak place in the cul-de-sac behind the site of operation unless proper steps are taken to avoid it.

I have also had some trouble with shortening of the vagina in operating for posterior vaginal enterocele. I should like to ask Dr. Phaneuf what means he uses to prevent this shortening of the vaginal canal?

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—It was mentioned a moment ago that the Mayo type of hysterectomy often leaves a defect between the uterosacral ligaments, and that statement is definitely true. When this operation is used, the surgeon should try, with the tissues under tension, to identify the uterosacral ligaments and bring them together accurately, down as close as possible over the rectum, especially in obese patients where the uterosacral ligaments are infiltrated with fat and the rectal wall is covered with fat.

Shortening of the vagina in these cases is an extremely important factor, for if the vagina is not shortened recurrence is very likely. Fortunately, the majority of these enteroceles occur among older women who probably are not so much concerned about vaginal shortening as they are about complete cure. I am very careful to state to the patient and her husband prior to surgical treatment that the vagina perhaps will not be as deep as it was before.

DR. PHANEUF (closing).—When he finds a beginning enterocele, Dr. Campbell places a purse-string suture around the sac, approximates the uterosacral ligaments and repairs the pelvic floor. This works satisfactorily in the earlier cases, but in the advanced ones I believe it is better to dissect and remove the sac, approximate the uterosacral ligaments, and repair the pelvic floor.

I agree with Dr. Kennedy that the term "enterocele" is a misnomer, and that "hernia of the cul-de-sac of Douglas" is a better one; yet, the term enterocele is used throughout the literature. The clamp method of vaginal hysterectomy, as advocated by Dr. Kennedy, has taken care of the enterocele as well as the prolapse of the uterus in a number of my cases, and it took Dr. Kennedy ten years to convince me of the value of this method. I have learned by experience that in the healing which takes place after a vaginal hysterectomy by the clamp method, the cul-de-sac of Douglas is pulled up by the keystone which is formed between the broad ligaments and the vaginal vault. I have employed this method especially in elderly women, who are in poor physical condition, and have seen them obtain relief from their enteroceles and prolapses.

Replying to Dr. Vogt's question as to the treatment of an enterocele in a patient who has had a vaginal hysterectomy, I would say this always offers a problem. What I do in such cases is to open the posterior vaginal wall longitudinally to the vaginal vault, resect the sac, or obliterate it by means of superimposed purse-string sutures, approximate the uterosacral ligaments, unite the crura of the pubococcygeus muscles to narrow the general hiatus, and repair the pelvic floor. This usually gives relief. The patients are enjoined against doing any heavy lifting or straining. Should there be a recurrence at a later date when these women have become older, a colpocleisis would, undoubtedly, take care of the lesion.

Dr. Counseller, like those of us who have operated on large enteroceles, finds that it is impossible not to shorten the vagina to some extent. This is something which the patient accepts if it is explained to her beforehand.

THE INVOLUTIONAL PHASE OF THE MENSTRUAL CYCLE (CLIMACTERIC)*†

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THE term "menopause" strictly applies only to the cessation of the menstrual periods, while the term "climacteric" refers to the period of reproductive regression and is to be preferred. Often this epoch is considered as a disease or syndrome, the process of living and associated influences not being considered. Under any circumstance and in either sex the five-year period (from 40 to 45 or 45 to 50) is a critical and exacting one. In the married female either the presence or lack of a family may be equally disturbing. The realization that the last chance of reproducing has passed, with the woman who desires a child, or the fear of pregnancy at this late date in a woman who has reared a family may disturb mental tranquillity. The childless woman who has not made adequate adjustment or the devoted mother who, with uncompensated grief, sees and feels her children breaking home ties, makes demands on natural reciprocity. The business of educating a family, seeing that it is favorably presented, and assuring it some degree of security is most exacting. The husband is a remarkable factor. The successes and failures over a period of years, the multiform problems that he has brought home, and, equally important, has not brought home, the precarious endeavor, at a time when his mental and physical agility often are incorrectly and prejudicially estimated, in trying for the last deal that will give economic independence all add doubt and worry to a varying and chaotic mind. These and many other reflecting factors make one realize that the climacteric is not a disease unless one considers living and the ageing process a disease. It also gives an insight into the probable inadvisability of routine substitutional therapy, given in an attempt to push back and withhold the natural gradual sequences associated with the climacteric.

Hormonology of the Climacteric

Ovary.—From many and varied observations we realize that there is a definite functional limit to the ovary. In the beginning increased refractivity to the pituitary gonadotropes which would manifest them-

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selves in failure of ovulation and resulting corpus luteum formation, which in turn would eliminate progesterone as a modifying influence on the gonadotropic secretion of the pituitary. At the same time the ovary might respond to the follicle-stimulating portion of the pituitary in which event one would expect bleeding from estrogenic endometrium when alterations in estrogenic levels occur. As these alterations become less pronounced, bleeding ceases. With the ovarian influence removed the cyclic function, qualitatively and quantitatively, of the pituitary is lost and the gonadotropic function is maintained at a higher and constant level.

Thyroid.—The behavior of the thyroid gland varies. In all probability there is increased thyrotropic influence from the less inhibited pituitary. It is noteworthy that symptoms of hyperthyroidism are often encountered at this time. However hypothyroidism may be noted, though not so frequently.

Pituitary.—Many functions have been ascribed to the anterior pituitary and many hormones have been thought to come therefrom. The pituitary is relatively a small organ and contains only several types of cells. It is situated in the middle of the skull where a slight increase in size or deviation from the normal would readily be interpreted in terms of headache, visual disturbances, x-ray findings, physical alterations, blood hormone changes, or other recognizable symptoms. How much simpler the problem would be if it could be shown that the anterior pituitary put out a "universal" hormone which served all the demands of growth, thyrotropic, gonadotropic, lactation, and other pituitary functions. There is a distinct probability that investigators have been "chipping off" portions of a hormone and carrying it in the direction of their research and interest. The alterations of the pituitary by other hormones, by depressing its function and probably by dilution, is more easily understood. It is our belief that histologically the pituitary is fairly constant.

Most of our attention in the past has been directed to the pituitary-ovarian relationship. Lately the role of the endometrium has been appreciated, and now it seems orderly and proper that the adrenal must be considered as a more integral part of sex endocrinology.

Adrenals.—The adrenal steroids have a similar chemical structure to the estrogens and it would seem that they might substitute for the lowered estrogens in an effort to depress and stabilize its relatively uninhibited pituitary. It also is likely that the medulla of the adrenal also is effected by this stimulation which would result in an increase of epinephrine. This could explain the well-known instability of the vasomotor systems in climacteric women, an instability which certainly is the chief indication for remedial measures.

Estrogenic ovarian failure, more severe in degree than that which occurs in many instances of intercurrent amenorrhea during the repro-

ductive period, occurs physiologically during the sexual ageing of woman or may be induced by radium or roentgenologic therapy. Complete ovarian deficiency occurs in bilaterally oophorectomized women. In all of these instances, the causes of the failure may be reduced to a simple common denominator, intrinsic ovarian damage, resulting from senility, radium, roentgen ray, or surgery. Patients with this type of intrinsic ovarian failure afford an excellent opportunity for the investigation of possible alterations in the androgenic functions of the adrenals secondary to ovarian deficiency or deprivation. If the findings reported upon patients with amenorrhea were interpreted correctly, studies of 17-ketosteroids excretion during the climacteric and after artificial menopause should show similar, if not more marked, elevations to those during amenorrhea.

Forty-one women during the climacteric or after artificial menopause were studied. They were grouped according to the cause and degree of ovarian failure incidental to this state. A total of 528 determinations was made, an average of 12.9 per patient.

In Group I, there were 12 women between the ages of 35 and 51 years, none of whom had ceased to menstruate, who had symptoms that are generally recognized as due to spontaneous estrogenic deficiency associated with the menopause. The average daily titer of these patients was 36 to 121 I.U. with a mean average for the group of 69 I.U., which represents an increase of 50 per cent over the normal. It is interesting to note that the group from 35 to 44 years had a mean average of 88 I.U., while the mean average of the group from 46 to 51 years was 43 I.U. which places emphasis on age rather than the actual cessation of menses in the compensatory adrenal activity.

In Group II, there are 5 women who had had radium or x-ray therapy from three months to three years previously. The average daily titer was 49 I.U. which is consistent with our ideas of ovarian impairment following the use of such agents. It is difficult to judge with certainty when one can expect absolute hypoovarianism from these procedures.

In Group III, there were 12 women who had complete ovarian failure from previous bilateral oophorectomies. In order to get more exact information, they were further divided into three groups according to the time of operation.

Group A comprised 5 women whose operations had been done nine to twenty-four days before the time of the collection of the last twenty-four-hour specimen for study. Their daily average of excretion was 25 I.U.

Group B comprised 5 patients whose operations had been done seven months to eight years previously, and in these patients the daily titers were increased to an average of 74 I.U.

Group C comprised 2 patients whose operations had been done sixteen years previously, and both of these patients showed normal excretion value of 40.

In Group IV, there were 12 women who had had normal physiologic menopauses. They also are divided into three groups according to the length of time since the cessation of menstruation.

Group A comprised 4 women whose ages ranged from 42 to 49 years and whose elapsed time since menstruation was from five to twelve months. The excretion values in these women averaged 77 I.U. or 64 per cent increase.

Group B comprised 5 women whose ages ranged from 48 to 57 and whose elapsed time since menstruation was from two to five years. The excretion values averaged 93 I.U. or almost 100 per cent increase over upper limit of normal.

Group C comprised 3 women whose ages ranged from 62 to 74 years and whose elapsed time since menstruation was from fourteen to twenty-six years. The excretion values averaged 39 I.U., which was within normal range.

An analysis of the data suggests the theory of ovario-adrenal reciprocities, which are influenced chiefly by way of the pituitary. During early life and until adolescence is well advanced, the adrenopituitary interchange is dominant in steroid metabolism. When primary or adolescent hypoovarianism occurs and is of sufficiently severe grade to result in failure of sexual maturation, this axis retains its dominant position even during adult years. Under these circumstances, the level of adrenal function remains about that characteristic of late preadolescence. Normally, however, with the advent of adolescence and the beginning of full ovarian function, the ovariopituitary interchange is superimposed upon the primordial adrenopituitary one. The result is a harmonious arrangement wherein the pituitary becomes conditioned to working with both adrenals and ovaries and to being influenced, as regards its functions by the regulatory effects of the intrinsic steroids of both the ovaries and the adrenals. During the reproductive period, the ovary and pituitary come to dominate the endocrine system. When, however, ovarian failure occurs from pathologic or physiologic causes, the pituitary, accustomed to being balanced in function by both the adrenal and ovarian steroids, is released in part from its inhibitions and, thereby, becomes hyperactive, then the adrenal cortex is stimulated to secrete greater quantities of steroids. The now dominant adrenopituitary interchange is stronger because of its previous conditioning by the ovary and pituitary. Eventually, however, stabilization occurs from the inhibiting effects of the increased amounts of adrenal steroids upon the function of the pituitary. The result is that during the late stages of sexual ageing and during somatic senescence, the adrenopituitary axis becomes stabilized and steroid output reaches normal levels.

Complications of the Climacteric

If there is any inherent weakness in the individual it is likely to become manifest at the climacteric. There are certain complications that are more often found and should be anticipated.

Irregular and Postmenopausal Bleeding.—The only natural and normal course of menstruation at this time of life is cessation. This may

be a gradual diminution of the amount at each period or a lengthening of the interval. In any event the trend should be toward stoppage. The basis for this was given in the discussion of the hormonology. Any departure from this course during or after the menopause must be investigated and due account given. The occurrence at this time of hyperestrogenic endometrial bleeding has been noted and the association of this with corporal carcinoma has been suggested. Curettement of the uterus and careful study is obligatory. Empiric endocrine and x-ray therapy is condemned and the removal of endometrial tissue for biopsy examination by the "punch" method is inadequate. In any event satisfactory diagnosis must be made for this type of bleeding.

In one year 1,089 women in North Carolina died of cancer. Of this number, 324 died of cancer of the uterus. In that year 15,732 females died in the State. This means that one woman out of every 15 died of cancer and that one out of every 48 died of cancer of the uterus. To state it another way, 196 more women in this State died from cancer of the uterus than from appendicitis. Seventy per cent were diagnosed only on admission to the Hospital.

Thyrotoxicosis.—This possibility must be investigated and eliminated before the blanket indictment of the "menopause syndrome" is made.

Psychoses.—One should remember that the business of living by this time (40 to 50 years of age) is beginning to make inroads and the exigencies of life are likely to become manifest. It is a recognized fact that women under certain circumstances and conditions, at this time may become melancholic. A noteworthy instance is the rural female, whose endocrinology, in all probability, is no different from that of her urban sister. One should dissociate the recognized and proved symptoms of the climacteric, such as vasomotor disturbances, from the psychic aberrations that are not peculiar to the sex.

The psychiatrists have cautioned that estrogenic therapy should not be exhibited unless one is treating definite symptoms such as "hot flushes." This in spite of the enthusiastic reports of the specific benefits of the estrogen in involutional melancholia. It is impossible to separate specific from suggestive therapy under these circumstances and as a matter of fact psychotherapy should be the first agent in treating a psychosis. There is a distinct possibility that organotherapy may be a distinct menace. Overzealous, indiscriminate or routine therapy, may result in bizarre symptoms and actual harm.

Vasomotor Symptoms.—In all probability vasomotor phenomena are the most consistent symptoms associated with the climacteric. As a matter of fact the frequency and severity of these symptoms are used as criteria for diagnosis and treatment. Since these are the most frequent and disturbing symptoms, therapy should be directed toward relief. The most frequent complaint is "hot flushes" or "flashes." This symptom is so consistent and well understood that it requires no

description. Sweating, dizziness, headache, and sleeplessness are other symptoms. Uncertainty, a sense of impending tragedy and various inchoate states may result. These can and should be anticipated. In fact anticipation, explanation, and preparation are the best therapeutic agents.

Therapy

First one should ascertain to his own satisfaction that he is actually dealing with symptoms of the climacteric. The keystone in therapy is making the woman acquainted with physiology of the process, an adequate stock taking, an explanation of what to expect, assurance of the temporary nature of the state, a discussion with the husband and adult members of the family, and a sincere assurance that you as a doctor and counsellor will be at hand for any service.

If our treatise is predicated on a sound basis, the first therapeutic agent called for should be psychotherapy. Simplified this means that we should take the time and trouble to make a definite diagnosis, rule out complicating factors, such as malignancy, and that we can sit down with our patient and devote such time to the discussion of her ailments as is necessary to put her mind at ease. When this is not enough we should resort to simple sedation and, in definite instances and under supervision, to organotherapy. In this event the estrogens are the logical choice. They should be kept at such a low level as not to cause endometrial stimulation with resulting uterine bleeding. Our preference is to give them by mouth and in a dose lower than usually prescribed. Emmenin 480 to 960 day oral units, or some other preparation in similar small doses may be given. Occasionally hypodermic medication may be required but here again the dose should be held at its minimum. Recently diethylstilbestrol has been accepted for inclusion in "New and Nonofficial Remedies" and the dosage recommended is 0.5 to 1.0 mg. It is our feeling that $\frac{1}{10}$ to $\frac{1}{2}$ this amount would give this necessary relief and would not be likely to cause uterine bleeding or influence the as yet unknown possibility of carcinogenesis. It is a potent therapeutic agent and its value is proved. It must be regarded as a potent agent.

Progesterone, in our hands, has been of little value in treating symptoms of the menopause.

If the generally accepted concept of the climacteric is true and if our quantitations of the 17-ketosteroids can be accepted, there is no place for androgen therapy at, or following, the menopause unless we wish to hasten or aggravate the process. Androgen therapy is predicated on its "estrogen negating." Such a state is flagrantly evident at this time. As yet no syndrome in the female has been ascribed, critically or otherwise, to a hypoandrogenic state. If this is true one should doubt the validity of its use in female endocrinotherapy.

The complications of the climacteric should and must receive primary consideration in therapy. Only after they, especially the possibility of cancer, have been evaluated should one outline definite treatment for the climacteric.

It is well to remember that muscle tone and sex steroid levels, especially the estrogens, have a relationship. There is a definite loss of tone and diminution in size of the organs, muscles, mucosa-supporting structure of the pelvis. Any pelvic repair or advice regarding repair should take account of this fact.

Summary

1. The term "climacteric," describing the period of normal reproductive regression, is preferable to the term "menopause," which simply designates the final menstrual period.

2. This epoch should not be considered a disease, unless the process of ageing and living is so considered. Neither should it be considered as entirely dependent and definite with ovarian failures. Many other factors, occult and manifest, influence the severity of the process.

3. The hormonology of the climacteric is now generally better understood. Refractivity of the ovary to pituitary stimulation, failure of ovulation, gradual lag in the response to follicle stimulation with receding waves of estrogenic output, a temporarily uninhibited pituitary with varying adrenal and thyroid stimulation is a brief summation.

4. The complications of the climacteric should be investigated before therapy is instituted. These are irregular bleeding, vasomotor phenomena, abnormal psychic states, thyroid disorders, pelvic relaxation, and systemic breakdowns.

5. The therapy should include practical and orthodox psychotherapy, explanation and correction of irregular bleeding, systemic treatment, necessary repair work, mild sedation and organotherapy.

6. Progesterone is of little value. Thyroid may be indicated. There is no indication for the androgens. Estrogen therapy has definite value. Preferably it is given by mouth in smaller doses than those usually prescribed. The daily dose of diethylstilbestrol, if used, should not exceed 1 mg. a day. Smaller doses are preferred and usually suffice.

Appreciation is expressed to Dr. E. C. Hamblen for the use of material that gives these observations a factual basis.

Discussion

DR. EMIL NOVAK, BALTIMORE, MD.—There is still a widespread tendency among practitioners, almost as much as among the laity, to ascribe to the menopause almost any nervous manifestation appearing in women over 40. Such symptoms are far more likely to be due to other causes, such as domestic or economic worries. To tell such women that they are "beginning to change" is the easy but the wrong way out, especially if it means resort to organotherapy, as too often it does.

The fundamental cause of the menopause is the cessation of ovarian activity. Because of the reciprocal, "seesaw" relationship between the ovary and the anterior hypophysis, cessation of estrogenic function means a relative increase of the pituitary gonadotropic function. By the administration of estrogens we can fill the estrogen deficiency, and let the patient down gently through this transition phase. Dr. Ross has properly emphasized, however, that the mechanism of this epoch may not be quite so simple as this, and that other endocrine glands, especially the adrenal cortex, may play an important role. The concept which he has presented of a phase of adrenal dominance following that of the ovary is a plausible and attractive one, and it may well prove correct.

While everyone now accepts the efficacy of estrogenic therapy for genuinely menopausal symptoms, we should remember that only a comparatively small proportion of menopausal women need any organotherapy at all. Many need only simple instruction and reassurance. Up to about twenty years ago gynecologists were likely to be either enthusiastic ductless gland faddists or hard-boiled skeptics. Looking back at this phase, the skepties were correct, for the preparations then available we now know were practically devoid of hormonal virtue. Now, however, we have at our disposal preparations of unquestioned estrogenic efficacy, and our results have improved correspondingly.

The introduction of the nonhormonal estrogenic substances, represented especially by diethylstilbestrol, has been a godsend to menopausal women, because of their efficacy by oral administration and their inexpensiveness. Certainly the incidence of unpleasant side-effects, in the small doses now advocated, is far less than the figures of 80 to 90 per cent formerly given by some authors.

There should be no such thing as a routine method of stilbestrol therapy, and I believe it to be bad practice to start a woman off on this drug and have her continue its use indefinitely, even though the dose is small. The drug should be given intermittently, and only when indicated by definite symptoms. Excessive or prolonged dosage carries with it the risk of producing bleeding, which may be a disturbing factor, especially in women who had ceased menstruating a year or two previously, because it must lead to the suspicion of adenocarcinoma. I have recently had sent to me sections of curettings following just this sequence of events. They showed a proliferative type of hyperplasia which had been diagnosed as adenocarcinoma by a competent pathologist. I believed the lesion to be entirely benign and advised repetition of the curettage a few weeks later, the stilbestrol having of course been discontinued. An amazing retrogression was revealed at the second curettage, the endometrium then being of the characteristic senile atrophic type.

DR. GEORGE F. PENDLETON, KANSAS CITY, MO.—What is your conception of why an ovary stops its activity at this time of life?

DR. NOVAK.—I think that can be about the same as to say why is a man's life three score years and ten. The ovary has a more or less foreordained life span and at the end of that time it comes to the end of its span of existence. This limited span of life is something innate in the mechanism and structure of the ovary.

DR. E. C. HAMBLEN, DURHAM, N. C.—I should like to emphasize the need for careful diagnostic studies when the problems of climacteric women are under consideration. The various symptoms of women of climacteric age cannot be related etiologically to the climacteric processes by recourse to chronologic considerations alone. In addition to a careful organic inventory designed to rule out intercurrent disease, the psychiatrist is often highly helpful in the evaluation of function at the psychic level. Many of the symptoms of climacteric women result more assuredly from psychic errors than from hormonal ones. Various involutional states, such as involutional melancholia, are not improved specifically by treatment with estro-

gens; indeed some are aggravated. A good principle to follow is: treat no climacteric woman with estrogens who does not count hot and cold flushes among her symptoms, although these vasomotor vagaries are by no means invariably pathognomonic of the climacteric.

DR. BAYARD CARTER, DURHAM, N. C.—There is one condition which has not been mentioned in which I think estrogenic therapy is highly valuable, and that is in women who have a prolapse. It has a particular advantage in the senile group of women who have put off operative procedures. I am convinced that preoperative estrogenic therapy makes the closure much more scientific and avoids surgery on their vaginal walls.

FACTITIAL PROCTITIS*

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MALIGNANT disease of the pelvic viscera of women, when sufficiently advanced, precludes the possibility of surgical operation; then treatment by radium or roentgen rays is required. Such treatment aims to destroy only the malignant tissue but sometimes the structure of other tissues exposed to the irradiation undergoes certain alterations. "Factitial proctitis"† is a term used to designate such a condition that is sometimes discovered in the wall of the rectum. Usually this lesion appears on the anterior wall of the rectum but in severe cases all walls may be involved. It varies in severity from mild inflammation of the rectal mucosa to complete dissolution of a portion of the rectovaginal septum. This factitial lesion may not be avoided in all cases. It does not indicate that poor technic has been employed. If treatment by irradiation will destroy or impede the malignant process, the possibility of proctitis occurring should not, and does not, interdict such treatment.

Pathology and Diagnosis

Following irradiation of some pelvic structures, usually the uterine cervix, induration and deformity develop in the tissues adjacent to the rectum. Palpation of the anterior wall of the rectum therefore may not give an accurate picture of the situation. If there is an ulcer it may be felt as an indurated crater, but often irregular thickening in the structures adjacent to the rectum will give the same impression, even when the wall of the bowel is intact. Factitial proctitis, not associated with formation of ulcer, cannot be detected by palpation. It is necessary to view the rectum by means of the proctoscope in order to detect the true nature of the condition of the rectal mucosa. When early

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†The term "factitial" is defined in Dorland's *American Illustrated Medical Dictionary*, page 535, "produced by artificial means; unintentionally produced."

factitial changes are present, only edema and diffuse reddening may be seen. The condition is encountered most frequently in a later stage than this, when bleeding from the rectum causes the patient to come for examination. By this time telangiectasis usually is present and is the cause of the bleeding. Often the reparative process of telangiectasis is noted early. The little, new blood vessels situated superficially in the rectal mucosa are broken by the slightest trauma. The anterior wall of the rectum, in its middle third, usually is reddened and studded with numerous capillaries. Merely swabbing this area lightly with a cotton applicator is sufficient to produce diffuse oozing of blood. Often it is necessary to defer examination on this account. In most cases the inflammation loses its intensity gradually but the process of healing is slow. After healing, the inflamed tissue is replaced by mucous membrane which possesses a yellow tint owing to deposit of scar tissue. Telangiectasis persists and, because of the vulnerability of these capillaries, bleeding from the rectum may occur from time to time over long periods. Indeed, in some cases in which the patients have been followed for years, this bleeding has continued to occur and it may persist as the only symptom of the condition. This presents an unfortunate problem. Many of the patients become "rectum conscious" and are never relieved of concern. These patients should present themselves for examination regularly.

The factitial ulcer is oval or irregularly circular and usually involves all layers of the rectal wall. Mobility of the diseased portion may be limited because of adherence to structures adjacent to it. The size of the ulcer averages from 1 to 3 cm. in diameter, the margins are smooth and regular in outline and the base, which is depressed, is covered with a silver gray or yellowish membrane, which is rough, slightly piled up and very tenacious and tough. The base of the untreated ulcer is covered with an ugly, slimy, greenish gray slough. Telangiectasis is always present in the mucosa surrounding the ulcer and with it various degrees of proctitis extend outward from the margin of the ulcer. Usually the ulcer is single. Occasionally there may be more than one. The inflammation and ulceration have a tendency to heal and, if the carcinoma does not terminate the patient's life, the factitial lesion usually will undergo resolution.

Symptoms

We have data on 88 cases in which significant symptoms led to proctoscopic examination and a diagnosis of factitial changes in the rectum following radiation therapy. These symptoms in order of frequency were most commonly bleeding from the rectum, frequent desire to go to stool, liquid stools, pain in the rectum, mucous discharges, and constipation. Other complaints that were made less frequently were of abdominal cramps, decrease in the size of the stool, and tenesmus.

The average time that elapsed between the initial course of treatment and the appearance of symptoms was ten months. Ten patients complained of various rectal symptoms that commenced immediately after treatment, and three patients noted the first symptom, bleeding from the rectum, thirty-eight, forty and forty-eight months, respectively, after the initial treatment.

Results of Examination

In 61 cases we know the type of pathologic lesion and the grade* of involvement for which treatment was administered. Fifty-one lesions were squamous cell epitheliomas of the uterine cervix; 3 were adenocarcinomas of the uterine cervix; 1 was a tumor containing both squamous carcinoma and adenocarcinoma; 1 was a primary carcinoma of the vagina; 1 was a papillary carcinoma of the ovary; and 4 were inoperable, extensive carcinomas of the uterine body. Seventeen tumors were found to be of Stage 4, 32 of Stage 3, and 12 of Stage 2. The grade of malignancy of the lesion and the amount of radiation given in each of these 61 cases is known. However, these data will not be presented because no useful correlation of them with the occurrence of factitial proctitis was ascertained.

The remaining 27 patients were among those who came to us after treatment elsewhere and in whose cases we were unable to verify the pathologic diagnosis. Of these, in 12 cases the neoplasms were judged clinically to be carcinomas of the uterine cervix of modified Stage 4; 6, of modified Stage 3; and 2, of modified Stage 2. In 7 cases it was not possible to learn why the patient had received irradiation.

Sixty of the 88 patients were examined through the proctoscope but once, for the reason either that they did not return to the clinic or that at a later visit, symptoms did not justify the examination. The remaining 28 patients were examined through the proctoscope two or more times over periods of two months to thirteen years. Twenty patients were examined twice, 4 patients were examined three times and 1 patient each was examined four, five, six, and seven times. The diagnoses made in the 88 cases are given in Table I.

TABLE I. DIAGNOSES MADE IN EIGHTY-EIGHT CASES

DIAGNOSIS	CASES
Factitial proctitis without stricture	39
Factitial ulceration without stricture	23
Rectovaginal fistula without stricture	1
Factitial proctitis with stricture	15
Factitial ulcer with stricture	8
Rectovaginal fistula with stricture	2

In 16 of the total of 88 cases, biopsy was performed and the diagnosis was inflammatory tissue in all but one, a case of primary carcinoma of the vagina.

The location of the factitial proctitis varied from just above to 20 cm. above the dentate margin, the average distance above this point be-

*The classification of lesions is that of the League of Nations, Health Organization, Cancer Commission: report submitted by the Radiological Sub-Commission. Geneva, *League of Nations Publications*, 1939.

ing 9 cm. In 6 cases the factitial involvement was diffuse and in the remainder it was circumscribed and located on the anterior wall of the rectum.

The factitial ulcers were found in the same area as the proctitis. The ulcers varied from 0.5 cm. in diameter to 6 by 4 cm.

In 25 cases reduction in the size of the rectal lumen was noted. This deformity involved the same portion of the rectum as the inflammatory and ulcerative disease already described. The lumen of the rectum was not reduced to less than 2 cm. in any case.

The site of rectovaginal fistulas was 5 to 6 cm. above the dentate margin. Two fistulas had occurred after radiation treatment of carcinoma of the cervix. In one other case a fistula developed after treatment of a primary carcinoma of the vagina.

Results

Thirty-two patients are known to have died of malignancy; 26 could not be followed and 30 were followed from eight months to thirteen years. Of these 30 patients who were followed, 25 noted marked improvement in the rectal symptoms after the acute stage of the condition subsided. Most of them experienced occasional bleeding from the rectum, some a tendency to constipation and one stated that the stool was reduced in size. Four patients stated that constipation was a considerable problem and one patient alive at the time of writing of this paper, four years after treatment had a rectovaginal fistula.

Illustrative Cases

CASE 1.—A woman, aged 50 years, had had one pregnancy. In January, 1940, a diagnosis of carcinoma of the uterine cervix had been made and treatment with radium and roentgen rays had been administered. In the course of the latter treatment she had experienced diarrhea, having as many as twenty-five discharges from the rectum each day. Following this there had been a tendency to constipation. In April she had been told that she had an ulcer in the rectum. She had experienced pain in the rectum but had noticed no bleeding.

In May, proctoscopic examination was performed. The lower half of the rectum was involved by an acute inflammatory process and the anterior wall, at the junction of the middle and lower thirds, was broken down into an ulcer 3 cm. in diameter. Severe pain was produced by the examination.

In October, proctoscopic examination did not cause pain. The condition of the rectum appeared much improved. At this time, the ulcer was about 2 cm. in diameter and much of the inflammatory change had disappeared.

In July, 1941, the patient related that occasionally some bright blood passed from the rectum, but there was no pain on defecation. On proctoscopic examination at this time, the area on the anterior wall, that had been the ulcer, was still of the same size but most of it had healed over. Telangiectasis was present. There was still, and probably always will be, general oozing of blood from the rectal walls.

CASE 2.—A woman, aged 46 years, had been pregnant twice. Diagnosis of squamous cell epithelioma, Grade 4, Stage 2+, of the uterine cervix

was made in August, 1936. Treatment by radium and roentgen rays was instituted. In June, 1937, she complained of diarrhea, rectal pain, passage of eight to ten stools a day, and occasionally bloody mucous discharge. The diarrhea changed to a fairly regular bowel habit but the bloody mucous discharge continued.

Proctoscopic examination in June, 1938, disclosed factitial proctitis with an area of ulceration measuring 1 by 2 cm. on the anterior rectal wall at a distance of 8 cm. from the dentate margin. This patient was examined with the proctoscope four times thereafter, the last time in May of 1941, when slight contraction of the lumen of the rectum was noted. The ulcer had healed. The rectal wall was the site of telangiectasis that produced slight bleeding when traumatized. The patient was essentially free of rectal symptoms.

Treatment

Except in those few cases in which ulceration is sufficient to lead to formation of fistula, or in the occasional case wherein actual involvement of the rectovaginal septum by the malignant process is responsible for breakdown of the tissues, healing will take place, providing the patient survives the malignancy for a sufficient time. Healing is accompanied by scarring, occasionally some reduction in the size of the lumen of the rectum and by telangiectasis which usually produces bleeding from the rectum. In cases in which strictures develop obstruction will not occur unless extension of the malignancy has been the cause of this stricture. Strictures resulting from proctitis do not offer a therapeutic problem very frequently.

Usually colostomy has not been considered part of the treatment of factitial lesions of the rectum. Those patients whom we have observed, on whom this operation has been performed, have obtained little relief from the pain, tenesmus and bloody mucous discharge.

Usually the patients can be taught proper care of the rectum. It should be explained to them that time is one of the most necessary factors to be considered and that treatment usually is prolonged. The patient should take a warm, cleansing enema after each defecation in order to keep the rectum as free from fecal matter as possible. She is then instructed to inject 2 fluidounces (60 c.c.) of warm hamamelis water (witch hazel), to be retained until the next movement of the bowel. Often the injection of 2 fluidounces of warm olive or mineral oil before retiring is of benefit. A bland diet, re-enforced with some substitutes to furnish bulk, such as are now available, allows a soft stool free from irritating particles. Caustic medicaments should not be applied.

The physician who must treat inoperable carcinoma of the female genital tract is confronted with a serious problem. His aim is to cure the malignancy or, if this is impossible, to obtain as much palliation as possible. In order to accomplish these effects he must irradiate the tumor intensively and yet afford the maximal protection to the neighboring

tissues not involved in the malignant process. However, should he be so cautious that he always avoids such incidental damage he may treat the neoplasm inadequately. Considering the very small percentage of patients treated with irradiation whose normal tissues sustain significant damage, and the gradual improvement in results following such treatment, it seems that factitial proctitis and ulceration, and the occasional rectovaginal fistula, must be accepted as risks that the patient should assume when such treatment is undertaken.

Discussion

DR. DAVID LUDWIG, PITTSBURGH, PA. (By invitation).—Our experience in postradium proctitis is limited to five in a series of 334 patients suffering from carcinoma of the cervix. Our observation covers a twenty-year period, although the 5 patients suffering from proctitis were treated in the last eight years. During this time 150 patients have been treated for carcinoma of the cervix. The average amount of radium treatment was 4,800 mg. hours, while the smallest dose given was 2,300 mg. hours. Divided doses were utilized in all patients receiving more than 6,000 mg. hours. In this series one patient developed ulceration without stricture, one had a rectovaginal fistula with stricture, and two proctitis without stricture.

One patient, a woman of 53 with a history of one pregnancy, will serve as an example. When first examined in November, 1935, there was an area of carcinoma on the right posterior vaginal wall about 4 cm. from the mucocutaneous junction. The past history showed, however, that in June, 1930, the patient had received 2,450 mg. hours of radium for adenocarcinoma of the fundus of the uterus. In October of that year complete hysterectomy was performed and the laboratory reported adenocarcinoma of the fundus of the uterus and chronic salpingitis. The patient reported also that she had been treated with small doses of radium a few months prior to our examination.

The carcinoma was now excised and the tissue reported secondary carcinoma of the vagina. Radium was given as follows: 8 radium seeds, 4 needles of 12.5 mg. each, and a capsule of 50 mg., totaling 2,060 mg. hours.

In April, 1936, a slough of the vaginal area with induration was observed. Proctoscopic examination showed that the anterior rectal wall was much reddened and slightly edematous with bleeding upon manipulation. Six weeks later there was a small area of ulceration although with treatment the patient was more comfortable than when the proctitis was first observed. In July, 1937, proctoscopic examination showed that the rectal mucosa was much improved. There was a small scar with slight bleeding upon manipulation. The patient has subsequently been examined on an average of every three months to August, 1942, at which time the vaginal mucosa was smooth and the rectum was healed with slight constriction of the lumen of the rectum.

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—This condition is not as rare as we are led to believe by the author's statements. If routine cystoscopic and proctoscopic examinations were done at one-, two-, or three-year intervals many cases of telangiectasia of the bladder and rectal mucosa would be found. Oftentimes symptoms due to these changes are not called to the attention of the physician.

The use of interstitial irradiation will increase ulceration of both the bladder and the rectum. Great care must be taken in packing these areas away from the source of irradiation, and we must remember when using multiple sources of radia-

tion that the beams may cross giving us a much higher dose of irradiation in the bladder or rectum than we are attaining in the lesion itself.

DR. WILLIAM A. COVENTRY, DULUTH, MINN.—I would like to report a case with this condition in which the patient had been maltreated before she came into my hands. She came from a small town in Wisconsin and had been treated by a country practitioner. She had been given, according to her story, 6,000 mg. hours of radium in the uterus and 1,200 mg. hours in the cervix some three months previously. When I first saw her she had an ulcer adjacent to the cervix and was almost a confirmed addict to morphia because of the severe pain. I attempted to treat her locally for three or four weeks, but the morphine habit and pain were getting worse and I then did a colostomy in order to put the rectum at rest. The pain disappeared in a week after I had diverted the fecal contents through the colostomy. She at that time developed a rectovaginal fistula at the site of the ulcer. In about three months the ulcer and rectovaginal fistula healed spontaneously and six months afterward I closed the colostomy. The patient has been observed for the last four years, and there is no sign of a return of the trouble. She gave up the morphine and gained in weight.

DR. FREDERICK S. WETHERELL, SYRACUSE, N. Y.—With the formation of many tumor clinics we are going to have more and more difficulties of the kind to which Dr. Randall has called attention. Radium in the minds of many men is merely a substance within a capsule which may be put into the cervical and uterine canal and left there for a certain number of hours to work a miracle. Sight is lost of the fact that it is distance, not filtration, which limits the action of the gamma ray, which explains the need for thick packs to displace rectum and bladder.

We as a Society should make a continued effort to limit the use of radium to men who are trained and who understand the physics of radium. A minor point in technique to many is the need of adaptation of the clinical picture to the method of dosage. Bowing of the Mayo Clinic, whose technique I have followed for twenty-two years, has had few cases of proctitis, due to the fact that he leans very much to the fractional method rather than the massive dose which was so prevalent twenty-two years ago. The only case of severe proctitis which I have seen was one which was treated entirely by x-ray, with a million volt machine. It was an advanced case and had been treated from the clinical experimental angle, quite properly.

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—Usually the best treatment of a severe irradiation burn is to cut out the burned area and implant a graft or flap of normal tissue. As such burns are precancerous lesions it would seem unwise to permit a patient to continue indefinitely with a severe irradiation proctitis. In a woman of 26 seen last year, a colostomy had finally been done to relieve the obstruction and local distress following intense irradiation for carcinoma of the uterus. The patient also did not wish to marry with a permanent colostomy, so we took out the remainder of the rectum, liberated the colostomized segment of the sigmoid and pulled it through the anus and closed the abdominal wound. This was a decided improvement. The possibility of a secondary cancer in the rectum, we believe, has been eliminated, the new anal opening is functioning and a very fair degree of control has developed, so that the patient need not wear a pad while the stools are formed. I would advise an operation of this type for another similar affliction.

DR. RANDALL (closing).—I believe that a majority of patients who have received treatment with radium and roentgen rays for carcinoma of the uterine cervix have factitial changes in the rectum. The group reported by us had sufficient symptoms to justify investigation by means of proctoscopic examination.

The patient to whom Dr. Coventry referred is one of the more fortunate individuals who have had colostomy performed. In those patients that we have seen in whom this operation has been performed, by no means all of them obtained the relief that had been anticipated.

Patients who have factitial changes in the rectum are frequently told that they have cancer in the rectum. In the group that we report this was true in only one instance, that of a case who had had a primary carcinoma of the vagina.

We were moved to write this paper to emphasize the fact that factitial changes are very common and must be accepted as one of the risks of adequate treatment of carcinoma of the uterine cervix.

EFFECTS OF ESTROGENIC THERAPY UPON OVARIAN FUNCTION*

II. When Employed During Anovulatory Cycles

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THE ability of adequate estrogenic therapy to transform normal progestational cycles of women to estrogenic (and presumably anovulatory) ones has been verified in the preceding communication.[1] It would appear most unlikely that therapy of this kind and order is capable of restoring normal progestational cycles in women with ovarian failure of anovulatory type.

An investigation, however, of the end results of estrogenic therapy in association with anovulatory failure seemed advisable for several reasons: (1) to confirm or to deny the dictum that, regardless of our ability to substitute for the endocrine deficiency of ovaries with intrinsic ovarian principles no salvage of physiologic functions, i.e., return of the fertile state, results; and (2) to confirm or to deny the theory that the salvage of ovarian function which has been described as following cyclic estrogen-progesterone therapy in a large group of women with prolonged or excessive estrogenic bleeding results solely from the estrogenic fraction of the therapeutic schedule. The commercial availability of a cheap, potent, and orally active nonhormonal estrogen (diethylstilbestrol) requires a clear definition of the role of estrogens in the treatment of ovarian failure.

Methods

Sixteen patients whose ages ranged from 15 to 35 years (average age 21.6 years) were selected for this investigation. These patients had presumed anovulatory ovarian failure predicated upon the occurrence of episodes of estrogenic bleeding. The bleeding cycles were commonly irregular and often of prolonged duration. Each patient selected had received from one to three endometrial biopsies prior to initiation of therapy.

Two hormonal estrogens, estriol glucuronide† and estradiol in the form of its benzoate‡ and dipropionate,§ and an nonhormonal estro-

*Part I of this article was included in the February issue.

†Estriol glucuronide (emmenin) supplied by Ayerst, McKenna and Harrison, Montreal, Canada.

‡Estradiol benzoate (progynon-B) supplied by Schering Corporation, Bloomfield, N. J.

§Estradiol dipropionate (di-ovocylin) supplied by Ciba Pharmaceutical Products, Inc., Summit, N. J.

gen, diethylstilbestrol,* were employed. Estradiol was administered intramuscularly, and estriol glucuronide and diethylstilbestrol were given orally. Their administration was of cyclic order, i.e., from the fifth to the fourteenth day of the cycles of 5 patients, and from the fifth to the twenty-fourth days of the cycles of 11 patients. Daily dosages varied: those of estradiol benzoate from 0.33 to 0.67 mg.; those of estradiol dipropionate 2.5 mg. every other day; those of estriol glucuronide from 1,800 to 4,800 oral units; and those of diethylstilbestrol from 1 to 3 mg.

Six patients received treatment during 1 cycle; 6 patients during 2 consecutive cycles; and 4 patients received treatment during 3, 4, 5, and 8 consecutive cycles, respectively.

Endometrial biopsies were done prior to, during, and after therapy. These biopsies were secured uniformly within the first twenty-four hours after the onsets of bleeding. Classification of endometrial responses was done by one of us (E. C. H.).

Data upon the lengths of the cycles and the durations and amounts of bleeding before, during, and following therapy were analyzed.

All patients had complete medical, gynecologic, and endocrine surveys, including determinations of the basal metabolic rate and roentgenograms of the sella turcica.

Data

The immediate effects of therapy were studied in 39 cycles. Following the cessation of treatment; clinical data upon 24 additional cycles were evaluated.

1. *Dosage Schedules.*—The therapeutic schedules employed and the related endometrial responses are detailed in Table I.

TABLE I. THERAPEUTIC SCHEDULES AND RELATED ENDOMETRIAL RESPONSES

	PATIENTS	CYCLES	ENDOMETRIAL FINDINGS	
			ESTROGENIC	PROGESTATIONAL
Estradiol benzoate:				
0.33 mg. 5th to 14th days inclusive	4	8	5	0
0.67 mg. 5th to 14th days inclusive	2	2	1	0
Summary:		10	6	0
Estradiol dipropionate:				
2.5 mg. every other day 5th to 29th days inclusive	1	1	1	0
Estriol glucuronide:				
1,800 o.u. 5th to 24th days inclusive	1	1	1	0
2,400 o.u. 5th to 24th days inclusive	2	3	3	0
4,600 o.u. 5th to 24th days inclusive	1	1	0	1
4,800 o.u. 5th to 24th days inclusive	2	2	2	0
Summary:		7	6	1
Diethylstilbestrol:				
1 mg. 5th to 14th days inclusive	4	5	3	0
1 mg. 5th to 24th days inclusive	2	2	0	1
2 mg. 5th to 24th days inclusive	8	11	4	2
3 mg. 5th to 24th days inclusive	2	3	2	0
Summary:		21	9	3

Total: 39 cycles of therapy; 26 endometrial studies, 22 estrogenic and 4 progestational.

*Diethylstilbestrol (estrobene) supplied by Ayerst, McKenna and Harrison, Montreal, Canada.

2. *Effects Upon the Endometrium.*—Endometrial studies were made during 26 of the 39 cycles of treatment of 12 patients. These findings are detailed in Table II. Twenty-two (84.6 per cent) of the 26 endometrial responses remained estrogenic. The 4 progestational endometriums encountered were in the cases of 2 patients, 3 in one instance and 1 in the other. One of these patients had progestational responses during the sixth, seventh, and eighth cycles of therapy (Fig. 1). All of her previously studied endometriums had been estrogenic. She had received previously estriol glucuronide, but at the time of her positive responses she was receiving diethylstilbestrol. The other patient had a progestational response after the fourth consecutive cycle of therapy with estriol glucuronide. Her 3 preceding cycles had been characterized by estrogenic endometriums.

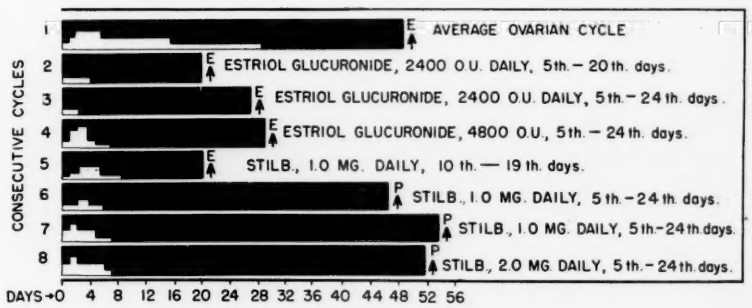

Fig. 1.—Effects of therapy with estriol glucuronide and diethylstilbestrol in 7 consecutive bleeding cycles of Patient 15. Episodes of bleeding are represented for each cycle at the left of the graph. *Stilb.*, signifies diethylstilbestrol.

TABLE II. ENDOMETRIAL RESPONSES DURING AND AFTER THERAPY*

CASE	SERIES OF THERAPY	CONSECUTIVE CYCLES STUDIED							
		1	2	3	4	5	6	7	8
1	1	edb-O	edb-E	edb-O	ORx-E	ORx-O			
2	1	edb-E	ORx-O	ORx-O					
3	1	edb-E	edb-E	ORx-O	ORx-O	ORx-O	ORx-O	ORx-O	ORx-O
4	1	edb-E	edb-E	ORx-O					
5	1	stb-E	stb-O						
6	1	stb-O							
7	1	stb-O	stb-E	stb-O	stb-E+				
8	1	stb-O	ORx-O	ORx-O					
9	1	stb-O							
10	1	stb-E	stb-E+						
11	1	stb-E	stb-E						
12	1	stb-E							
13	1	edb-O	stb-O						
14	1	edd-E	ORx-E	ORx-O	ORx-O	ORx-O	ORx-E-		
	2	stb-O							
15	1	edb-O	es-E	es-E	es-E	stb-E	stb-P-	stb-P-	stb-P
16	1	es-E	es-E	es-E	es-P	stb-O			

**Therapy*

edd, Estradiol dipropionate
edb, Estradiol benzoate
es, Estriol glucuronide
stb, Diethylstilbestrol
ORx, No therapy, but data on cycle and bleeding obtained

Classification of Endometrial Responses

E–, Minimal estrogenic response
E, Moderate estrogenic response
E+, Marked or hyperestrogenic response
P–, Minimal (immature) regular progestation
P, Normal progestation
O, No biopsy

Few endometrial studies were made following cessation of therapy due to the fact that the majority of the patients were transferred to other therapeutic regimen. Three follow-up endometrial samples, however, were taken on two patients; all were estrogenic.

3. *Effects Upon the Lengths of the Cycles.*—The characteristic effect was a reduction in the cycle lengths to within normal limits: the average lengths of cycles prior to treatment were 49.2 days and during therapy 28.7 days. This effect was apparent in the first treatment cycles which averaged 33.1 days in length. In 2 instances, however, estradiol therapy was followed by absence of expected episodes of bleeding with sequential doubling in the lengths of the cycles. Both of these exceptions occurred during first treatment cycles and are included in the above average of 33.1 days.

Following the cessation of treatment, data on 6 patients indicated a regression from the established normal cycle lengths, the average becoming 48.5 days.

4. *Effects Upon the Duration and Amount of Uterine Bleeding.*—The average duration of bleeding decreased from 18.4 days prior to treatment to 6.2 days during therapy. This alteration was immediately apparent in the first episodes of bleeding which occurred during therapy.

Episodes of bleeding following cessation of therapy averaged 7.2 days. During the cycles studied after therapy only 1 patient had a recurrence of prolonged bleeding. This occurred at the termination of the second cycle which followed the cessation of therapy. This patient had received only 1 cycle of diethylstilbestrol therapy, 2 mg. daily, from the fifth to the twenty-fourth days, inclusive.

Prior to therapy an average of 46 well saturated sanitary pads were used per episode of bleeding, during therapy 13, and following cessation of treatment, 15 per episode of bleeding. The reduction in the total number of pads used by these patients during treatment paralleled the decrease in the duration of bleeding.

5. *Effects Upon Withdrawal Time.*—An episode of bleeding was defined to be due to estrogen withdrawal if it occurred within a few days after cessation of therapy and considerably in advance of the expected date of bleeding. In 6 treatment cycles of 4 patients the withdrawal time averaged 4.5 days, the range being from two to eight days. Three of these patients had received estradiol benzoate during the first half of the cycle while the fourth patient had received diethylstilbestrol during the same interval.

Discussion

There is little evidence from the data presented that the use of moderately small doses of hormonal or nonhormonal estrogens exerts stimulative or restorative effects upon the disturbed ovario-endometrial status of anovulatory ovarian failure. Of 26 endometrial responses studied during therapy 22, or 84.6 per cent, were estrogenic.

The 4 progestational responses encountered in the instances of 2 patients warrant discussion. The therapeutic schedules of these 2 patients have two things in common: (1) They were of greatest length (5 and 8 consecutive cycles); and (2) they comprised 3 consecu-

tive cycles of estriol glucuronide therapy. The progestational response of one patient followed the third cycle of estriol glucuronide therapy but did not recur in the succeeding cycle of diethylstilbestrol therapy. The 3 progestational responses of the other patient occurred during the second, third, and fourth consecutive cycles of diethylstilbestrol therapy, which were sequential to the treatment with estriol glucuronide. These progestational responses may be regarded as being the results of intercurrent recovery of ovarian function or one may relate their incidence to a specific virtue of prolonged therapy with estriol glucuronide. Therapeutic schedules of this kind and order warrant further study.

The estrogenic therapy was observed to regulate quite uniformly the cyclicity and duration of flowing. The majority of the patients studied had lengthened cycles (average 49.2 days) and prolonged flowing (average duration 18.4 days) prior to institution of therapy. During therapy the cycle lengths were reduced to an average of 28.7 days and the durations of bleeding episodes to an average of 6.2 days.

From these studies, it seems reasonable to relate chiefly the regulatory effects of cyclic estrogen-progesterone therapy in prolonged or excessive estrogenic bleeding to specific effects of the estrogen fractions on the endometrial vascular system. The ultimate salvage, i.e., return of progestational cycles, which has been related to this cyclic combined therapy seems dependent upon the one-two sequential use of and the synergism existing between estrogen and progesterone. It is doubtful that any direct stimulative effects upon ovarian function result but rather it is likely that intercurrent recovery is facilitated and progression of ovarian failure prevented by the regulatory actions of this therapy on the functional capacities of the endometrial vascular tree and the pituitary.

Summary and Conclusions

Moderately small doses of hormonal estrogens (estrone, estradiol benzoate and dipropionate, and estriol glucuronide) and of a nonhormonal estrogen (diethylstilbestrol) were administered cyclically to 16 women who were experiencing anovulatory ovarian failure predicated upon the occurrence of prolonged and excessive estrogenic bleeding. Twenty-two of the 26 (84.6 per cent) endometrial biopsies studied during therapy continued to be of estrogenic nature. The 4 progestational responses, which were encountered in 2 patients, were related to prolonged therapy with estriol glucuronide and were judged to be evidence of intercurrent recoveries of function. Satisfactory regulation of the cyclicity and duration of flowing was credited to the cyclic estrogenic therapy.

The following conclusions are judged warranted:

1. The cyclic administration of moderate doses of hormonal and nonhormonal estrogens resulted in no direct stimulational effects upon ovaries in anovulatory failure.

2. Therapy of this kind and order regulates the cyclicity and duration of flowing probably by direct alterations in the functional capacities of the endometrial vessels.

3. The regulatory action of cyclic estrogen-progesterone therapy is due primarily to effects of the estrogen fraction.

4. The salvage of physiologic function which occurs in many patients with estrogenic flowing following therapy with the cyclic estrogen-progesterone schedule is dependent upon the progesterone fraction.

5. The one-two administration of and the synergism between estrogens and progesterone are important facets of the combined therapy.

6. Salvage, when it occurs, probably is due to the ability of this complemental therapy to prevent progress of ovarian failure and to favor spontaneous recovery of normal function.

Part of the expenses of these studies was defrayed by grants to one of us (E. C. H.) from the Research Council of Duke University, from Ayerst, McKenna and Harrison, Ltd., Montreal, Canada, and from Schering Corporation, Bloomfield, N. J.

Reference

1. Hamblen, E. C., Hirst, D. V., and Cuyler, W. K.: Am. J. Obst. & Gynec. 45: 268, 1943.

THE MANAGEMENT OF OVARIAN TUMORS IN ELDERLY WOMEN*

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SURGERY in elderly women, especially in the seventh, eighth, and ninth decades of life, is attended with considerable risk. Many such patients present themselves at a hospital or a clinic with ovarian tumors, but because of their age or poor physical condition, they are denied the benefits of surgery. Although most gynecologists agree that the only chance these patients have to be cured is by operation, frequently they feel that the additional life expectancy does not warrant the procedure. Our experience at Kings County Hospital has been at variance with this. We present, therefore, a brief summary of our results in the management of ovarian tumors in women past the menopause.

From Jan. 1, 1935, through July 1, 1942, a period of seven and one-half years, 13,010 patients were admitted to the gynecologic service of the Long Island College Division of the Kings County Hospital. Of this number, 344, or 2.6 per cent, had ovarian tumors. Pathologic study revealed practically all varieties (Table I), and 262, or 76.2 per cent, were benign, while 82, or 23.8 per cent, were malignant. Eighty-

*Read at a meeting of the Brooklyn Gynecological Society, Nov. 6, 1942.

eight, or more than one-fourth of the patients, were fifty years of age or older, while 10 were more than sixty-five years (Table II). In the postmenopausal group, 27, or 30.7 per cent, of the tumors were benign while 51, or 69.3 per cent, were malignant.

TABLE I. CLASSIFICATION OF OVARIAN TUMORS

TYPE OF TUMOR	TOTAL	POSTMENOPAUSAL	
		NUMBER	INCIDENCE (%)
Benign:			
Simple serous cystadenomas	196	24	12.3
Papillary serous cystadenomas	5	2	40.0
Pseudomucinous cystadenomas	21	5	23.8
Dermoid cysts	32	2	6.3
Fibromas	4	1	25.0
Granulosa cell tumors	2	2	100.0
Thecomas	1	1	100.0
Brenner cell tumors	1	0	0.0
Total	262	27	30.7
Malignant:			
Adenocarcinomas	78	47	60.3
Krukenberg tumors	4	4	100.0
Total	82	51	62.2
Grand Total	344	88	25.6

TABLE II. AGE INCIDENCE

	51-60		61-70		71-82	
	BENIGN	MALIGNANT	BENIGN	MALIGNANT	BENIGN	MALIGNANT
Number	16	36	5	19	6	6
Incidence	18.2	39.8	5.7	21.6	6.8	6.8

From this it is apparent that more than one-fourth of the women admitted to our institution with ovarian tumors after the menopause could be cured by surgery, provided the procedure was carried out with a minimum of shock and trauma, either from the operative procedure itself or from anesthesia. It is true that in this age group, patients are frequently more prone to have chronic cardiovascular, pulmonary, or renal diseases, but these complications have not been sufficient to contraindicate an attempt at surgical removal of the ovarian mass.

In the management of such patients, three cardinal principles must be adhered to: (1) careful, preoperative preparation; (2) rapid operation with minimum trauma; (3) early return to activity.

To evaluate the surgical risk, close cooperation with the department of medicine is maintained. Routine preoperative chest plates, electrocardiograms and detailed renal function studies are essential. A preliminary period of bed rest is often necessary; in several of our cases, a period of two months was employed. Where necessary, transfusions, and fluids should be liberally given. Digitalis is administered for signs of decompensation or myocardial damage. Careful watch of the blood count, sedimentation time, and the temperature determine the optimum time for surgery, and, when this time arrives, the operative procedure

selected is the simplest and most rapid which will eliminate the pathology. To avoid the ill effects of general anesthesia, local anesthesia is used exclusively.

Procedure

All patients are premedicated with twilight sleep (morphine sulfate and scopolamine hydrobromide), the dose being determined for each individual according to age, general body configuration, and physical condition. The average dose required was a total of one-third grain of morphine sulfate and one one-hundredth grain of scopolamine hydrobromide given in divided doses. In only a few instances was it necessary to resort to supplemental inhalation anesthesia. Local anesthesia demands extreme gentleness and care in the handling of tissues, and this, we believe, is ideal for such patients. If the patient's condition is satisfactory at the close of the operation, closure of the abdominal wall is performed in layers using interrupted, nonabsorbable, fine sutures (silk or cotton). This method of closure requires minimal handling of tissues and results in little or no local tissue reaction. However, if the patient's condition is poor, the abdominal wall is closed with heavy through-and-through, nonabsorbable sutures that are carried through all the layers from peritoneum to skin, inclusive. Postoperatively, the prevention and early treatment of distention lessens cardiac embarrassment and discomfort. Prostigmine is used routinely for this purpose. Fluids and food by mouth are started within a few hours after the patient's return to bed. Only in rare instances have we had to use cardiac stimulants other than digitalis. The patient is encouraged to move her legs and is not permitted to remain in one position for more than an hour. All efforts are made to get her out of bed as soon as possible. This has been facilitated by the careful closure of the abdominal wall with nonabsorbable sutures, supplemented by a good abdominal binder.

To illustrate these principles, we have chosen the following typical case:

Case Report

Mrs. J. A., a 65-year-old, white housewife, was admitted to the gynecologic service of the Long Island College Division of the Kings County Hospital on April 25, 1938, complaining of progressive abdominal enlargement and left lower quadrant pain, accompanied by marked urinary frequency. These symptoms had been present for two months. Her menopause occurred fifteen years before, and since then she has had no bleeding or vaginal discharge. The significant findings on physical examination were an elevated blood pressure (160/85), a moderately enlarged heart with a systolic murmur at the apex, and a large, cystic, indefinite mass which arose from the pelvis and filled the lower half of the abdomen. After preliminary study and bed rest for ten days, during which time she was digitalized, laparotomy under twilight sleep and local anesthesia was performed. A 20 cm. multilocular, pseudomucinous ovarian cyst was removed and the abdomen was closed in layers with fine black silk. The total operating time was fifty minutes. Her postoperative course was uneventful. The highest temperature was 100.6° F. on the second postoperative day. She was allowed out of bed on the fifth day and discharged as cured on May 21, 1938, sixteen days after the operation.

Results

The results of this routine have been most gratifying to us. There were no mortalities among the 25 women operated upon where benign neoplasms were found. Two patients died before operation, one from bronchopneumonia and the other from cardiac failure. Many of these women have been followed for five or more years and at present are well and asymptomatic. As is to be expected, the mortality was considerably higher in the group of 51 malignancies. However, the immediate postoperative failures were comparatively few. Only three patients failed to survive the immediate postoperative period. One patient died from renal insufficiency, the second from bronchopneumonia on the eighth postoperative day, and the third from cardiac failure. More than half of the patients followed (57.6 per cent) died within five years. Nevertheless, considering the fact that most of these women were originally sent to the Kings County Hospital for terminal care, since operation was deemed impossible or foolhardy, even this low salvage rate is worth while.

Consequently, before condemning an elderly woman with an ovarian tumor to a short life of chronic invalidism, it behooves the physician to remember that in our experience, one-fourth of the patients had benign lesions, although the preoperative diagnosis was usually ovarian malignancy. With proper caution, such women were returned to a normal, active, self-sustaining life to which at least five years have been added. To refuse the benefits of surgery to an elderly woman purely on the basis of her age or moderately poor physical condition, in our opinion, is not justified.

Summary

1. A brief summary of 344 cases of ovarian tumor is presented.

2. Attention is called to the fact that in 88 neoplasms found in women of fifty or more years of age, 30.7 per cent were benign, and with proper precautions, they were successfully removed.

3. The routine for the care of this group is outlined.

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PATHOLOGY OF POSTMENOPAUSAL BLEEDING*

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THIS report is based on the pathologic findings in women 50 years or older, or past the menopause, who presented themselves at the Kings County Hospital, Long Island College of Medicine Division, for vaginal bleeding, spotting, or staining. It includes all specimens in the above category, received in our laboratory from December, 1939, to December, 1941. The total number of specimens reported is 114, selected from over 2,000 gynecologic specimens received during this period. Clinical consideration, other than brief mention, is beyond the scope of this paper.

The minimum age limit of 50 is selected to avoid bleeding due to fibroids, and to study the pathology of the endometrium in this age group. Only a short discussion will be devoted to the malignancies encountered in this survey; the remainder of the report will be concentrated on benign causes for postmenopausal vaginal bleeding, or bleeding in women past 50.

There were 42 cases of malignancy representing 36.8 per cent of the total; 23 were carcinoma of the cervix (20.2 per cent) and 19 were carcinoma of the corpus (16.7 per cent). In two patients, vaginal bleeding was associated with ovarian tumors; one, in a patient aged 61 years, was a thecoma, and the other, in a patient aged 53, was a papillary adenocarcinoma. In addition, 6 cases were associated with extra uterine pathology; 3 metastatic malignancies from unknown origins, one neurogenic sarcoma, one carcinoma of the vulva, and one mixed mesodermal tumor of the uterus. The total incidence of malignant lesions equals 43.1 per cent (corrected for one benign ovarian tumor).

In the remaining 65 cases (56.9 per cent excluding the thecoma), vaginal bleeding was either associated with benign lesions of the endometrium or cervix, or no demonstrable cause was evident.

There were 6 cases of endocervicitis; one associated with endometrial hyperplasia, and the etiology for the bleeding was ascribed to the hyperplasia. There were 5 cases of benign cervical polyps, and 4 of endometritis.

In 10 instances, insufficient material was obtained for diagnosis; nevertheless, these women had vaginal bleeding. In one, the diagnosis was found to be an adenoma malignum after the uterus was obtained.

Atrophic endometrium was diagnosed twice. One was associated with a large endometrial polyp presenting hyperplastic changes, and this readily accounted for the bleeding; this patient was 50 years old. The

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other was in a 60-year-old woman who had an endocervicitis which probably caused the anomalous bleeding.

In 21, the findings were those of a cyclic mucosa: 15 were in the proliferative and 6 were in the secretory phase. Of these, 7 were associated with endometrial polyps, 5 with fibroids, and 2 with malignancies of the cervix. The ages of these patients varied between 45 and 60 with an average of 51. They were five months to five years past the menopause. Endometrial polyps alone were found in 8 cases; in 5, concomitant hyperplasia of the endometrium was found with the polyps.

A striking finding in this series was 8 cases of endometrial hyperplasia representing 7.0 per cent of the total. The ages of the patients varied between 47 and 81 with a mean of 55 years, and the patients were 15 months to 30 years postmenopause. The bleeding was usually more constant and more profuse, and varied over a period of time. The cause for hyperplasia in elderly women is speculative, as is the reason for cure of their vaginal bleeding by curettage.

TABLE I. MALIGNANT LESIONS

	NUMBER OF CASES	INCIDENCE (PER CENT)
Carcinoma of cervix	23	20.2
Carcinoma of corpus	19	16.7
Metastatic malignancy of uterus	3	2.6
Mixed mesodermal tumor of uterus	1	0.9
Malignancy of ovary	1	0.9
Carcinoma of vulva	1	0.9
Neurogenic sarcoma	1	0.9
Total	49	43.1

TABLE II. BENIGN LESIONS

	NUMBER OF CASES	INCIDENCE (PER CENT)
Cyclic mucosa,	21	18.4
proliferative,	15	13.2
secretory	6	5.2
Undetermined	10	8.8
Endometrial hyperplasia	8	7.0
Endometrial polyps	8	7.0
Endocervicitis	6	5.2
Cervical polyps	5	4.3
Endometritis	4	3.5
Atrophic mucosa	2	1.8
Benign ovarian tumor (thecoma)	1	0.9
Total	65	56.9

Breipohl,[1] in 1935, reported a study of 130 postmenopausal endometriums. A large number showed changes of the atrophic type; adenocarcinoma was seen in 22; 31 were proliferative, of which 15 were hyperplastic (including 2 granulosa cell carcinomas), and 3 secretory.

Taylor and Millen,[2] in 1938, found 63 per cent of postmenopausal bleeding associated with some form of carcinoma. Included in their series of benign lesions of the endometrium were 74 cases diagnosed as atrophic mucosa, and 11 as hyperplasia (4 of these were associated with granulosa cell tumors).

In 1941, Novak and Richardson, Jr.,[3] reported 137 cases of postmenopausal endometriums; 62 were diagnosed as atrophic, 14 moderately proliferative, 28 actively hyperplastic, and 33 were of the retrogressive hyperplastic type ("Swiss-cheese" pattern with a low atrophic epithelium and a fibrous stroma).

Geist and Matus,[4] in 1933, in a series of 182 cases of postmenopausal bleeding found that 42 per cent were benign. Ovarian neoplasms were found in 10; 29 were due to polyps; 10 associated with hyperplasia; 11 were inflammatory (endometritis or endocervicitis); 15 had fibroids; 3 had adenomyosis, and 13 were negative.

Our findings are not consistent with those cited above nor with other reports in the literature. The percentage incidence of malignancy and the number of specimens diagnosed as atrophic endometriums in our series is appreciably less.

TABLE II. SUMMARY

	NUMBER OF CASES REPORTED	MALIGNANT LESIONS (PER CENT)	BENIGN LESIONS (PER CENT)
Kanter and Klawans[5]	98	68.4	31.6
Brown[6]		66.8	33.2
Schulze[7]		68.0	32.0
Geist and Matus[4]	182	57.5	42.5
Norris[8]		53.3	46.7
Taylor and Millen[2]	406	63.3	36.7
Te Linde[9]		53.3	46.7
Geiger[10]	395	81.3	18.7
Schwartz (1942)	114	43.1	56.9
Average		61.6	38.4

Discussion

Bleeding from an endometrium that is neither being sensitized, nor undergoing cyclic changes because of cessation of ovarian function, is an interesting phenomenon and at present has not been satisfactorily explained. It is true that many are associated with malignant growths, and in a relatively large group the underlying factor may be an inflammatory process or a benign neoplastic growth, or as has been shown above, no lesion whatever can be demonstrated.

The exact cause for the activity of the endometrium in elderly women is not understood, since the source of postmenopausal estrogen is not precisely known. Regressive changes and diminished function in the ovary occur before the menopause becomes evident. Scars and furrows on the ovary increase in number as follicles rupture and are transformed to corpora lutea and corpora albicantia. The number of mature follicles decreases and the atretic follicles regress and occasionally leave small scars.

Blood and urine assays of ovarian hormones during the climacteric have been reported, but no complete study of secretion and excretion of these hormones during this entire period has been carried out. It is generally accepted that secretion of estrogens diminishes up to the menopause, and thereafter continues at a much reduced level.

The ovary is not capable of spontaneous reactivation after the menopause, and, therefore, some other mechanism or source must be found for the estrogens. Of all the possibilities, two seem most likely. The estrogenic sex sterols are chemical metabolites of certain body sterols with cholesterol as the mother substance of the estrogens. Or an extraovarian endocrine gland, most likely the follicle-ripening gonadotropic hormone of the anterior pituitary may be the source. In favor of the latter is the presence of the estrin factor in the urine of castrated women, but this evidence is only presumptive and has a wide individual variation.

Conclusion

The varied histology of the endometrium after the menopause reflects the variation in the terminal functional activity of the ovary. If menstruation and ovulation end together and abruptly, the endometrium will be of the atrophic type. If the terminal cycles are anovulatory, the hyperplastic pattern may exist even in the absence of postmenopausal bleeding. After estrogenic production ceases, the pre-existing hyperplasia may show marked regressive changes in the epithelium and stroma.

Summary

1. The pathology of 114 specimens from women past the menopause or over 50 years of age who had anomalous bleeding is reviewed.

2. The percentage of benign lesions of the endometrium or cervix is 56.9, and the percentage of malignancy is 43.1.

3. Endometrial hyperplasia represented 7.0 per cent of the total.

4. The cause for postmenopausal bleeding cannot always be determined.

5. The histology of the postmenopausal endometrium depends on the terminal functional activity of the ovary.

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RÉSUMÉ OF CARDIAC DISEASE IN PREGNANCY FOR A FIVE-YEAR PERIOD*

With Report of a Case of Coarctation of the Aorta

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IN REVIEWING the chronic cardiac patients among the pregnant women cared for on our service at this hospital during the past five years, we find from Table I that they numbered 102 out of a total of 5,664 deliveries, or 0.18 per cent.

TABLE I

	CARDIAC CASES	WARD	PRIVATE	SECTIONS	INTERRUPTED	DEATHS
1937	23	17	6	1	0	1
1938	30	22	8	3	1	0
1939	21	13	8	0	1	0
1940	12	9	3	3	0	0
1941	16	11	5	0	3	0
Total	102	72	30	7	5	1

Ninety-six of the 102 were delivered from below, usually by low forceps to shorten the second stage in both multiparas and primiparas alike. Seven were delivered by cesarean section. Of the seven cesarean sections, one was private and six were service patients. Four were primiparas and three multiparas. Two were repeat sections. Indications were active chorea and rheumatic heart disease, previous decompensation, coarctation of the aorta, marked cardiac enlargement with double lesion and probability of very long labor in a primipara with double lesion. There were three therapeutic interruptions in the first trimester, two by abdominal hysterotomy with sterilization, and one from below. There was one death. This followed cesarean section under local, supplemented by cyclopropane anesthesia and was due to pneumonia. There have been two general trends evident in our handling of these cardiac patients. One, the tendency to deliver more and more cardiac patients from below rather than by section. Two, the tendency to substitute cyclopropane anesthesia for the time-honored open drop ether in cases delivered from below, and local in sections.

The most unusual of these cases was one of coaretation of the aorta, and as only 29 cases of this complication in pregnancy had been reported in the literature up to 1940, it was thought that a report of our case might be of interest.

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J. T., a 20-year-old white secundigravida, para 0, was admitted to the prenatel cardiac clinic in the fifth month of her pregnancy because of hypertension and a cardiac condition noted in the obstetric clinic. Except for occasional headaches, she felt well. She could climb three flights of stairs before becoming dyspneic. There was no orthopnea, precordial pain, palpitation, or edema. She had not been aware of hypertension up to this time. A previous pregnancy had terminated in a spontaneous abortion at two months. There was a history of rheumatic fever at the age of 10 and a recurrence of this disease at 18. After the initial attack, exercise had been restricted because of a heart condition.

Physical examination showed the patient to be free of any distress. Her face was ruddy. Temperature, pulse and respirations were normal. She weighed 130 pounds and was 5 feet 7½ inches tall. Blood pressure was 172/92. Blood Wassermann and urine were negative. Pelvic measurements were normal. The thyroid was symmetrically enlarged to about twice normal size. There was a marked pulsation visible in the suprasternal notch. Lungs were clear. The cardiac apex impulse was palpable in the midclavicular line. On auscultation, the heart sounds were of good quality and there was regular sinus rhythm. A loud, high-pitched systolic murmur was audible in the left third intercostal space and was transmitted upward to the right clavicle. A rasping systolic murmur was heard over the back at the level of the scapula. The aortic second sound was accentuated. The blood pressure of the lower extremities recorded at the popliteal space was 122/90. The femoral pulse on either side did not lag appreciably behind that palpable at the wrists. There was no clubbing of the fingers or toes and no edema.

A 6-foot teleroentgenogram of the chest showed no enlargement of the heart. The pulmonary arc was accentuated and the arch of the aorta was small. The lower margins of several ribs on the right side suggested pressure erosion. The transverse diameter of the chest measured 26.7 cm., that of the right heart 4.6 cm. and that of the left 8.6 cm. The total transverse heart diameter was 13.2 cm. The cardiothoracic ratio was 49 per cent. The vascular pedicle measured 5.1 cm. Fluoroscopy confirmed the above findings and showed the aorta to be smaller than normal and somewhat elongated. An electrocardiogram showed only a slight degree of sinus arrhythmia present. Diagnosis of the cardiologist was: Congenital heart disease and rheumatic heart disease, coarctation of the aorta, and normal sinus rhythm, Class I-C.

Because the patient was well along in the second trimester, it was advised that her pregnancy be allowed to continue nearly to term and then be terminated by cesarean section, with sterilization at that time.

Under strict supervision, of both obstetric and prenatal cardiac clinics, she was carried to within three weeks of the expected date of confinement without any untoward signs or symptoms. The blood pressure remained high, ranging between 146/62 and 172/88. Repeated urinalyses were entirely negative.

On admission to the hospital Oct. 15, 1940, the blood pressure in the left arm was 176/106. In the left leg the blood pressure was 110 systolic and diastolic could not be elicited. The fundus contained the breech and was 4 fingers below the xiphoid. The vertex was movable above the brim of the pelvis, back on the left, small parts right. Fetal heart was regular and heard best on the left. By rectal examination, the cervix was soft, thick, and closed; the vertex could barely be reached.

Blood studies were recorded as follows: Hemoglobin, 70 per cent; red blood cells, 3,500,000; white blood cells, 5,000 with 82 per cent polymorphonuclears and 18 per cent lymphocytes; Blood urea 14.2 mg. per 100 c.c., creatinin 0.59 mg. and sugar 75 mg. The sedimentation rate was 36 mm. in ½ hr. and 73 mm. in 1 hr. The circulation time with patient in the recumbent position and using 5 c.c. of decholin injected into the right anticubital vein was 12 sec. (normal 14 to 16 sec.). The same amount in the ankle vein was 32 seconds.

Except for slight stiffness and narrowing of the veins, the eye grounds were negative.

Six days after admission, a low flap cesarean section and Pomeroy sterilization were performed. A living male infant weighing 7 pounds and 8 ounces was delivered. Pitocin was used as an oxytocic. Preoperative medication consisted of 3 grains of seconal and 1/150 grain of atropine. Local infiltration and block anesthesia using ½ per cent novocain without adrenalin were used and supplemented by intravenous sodium pentothal. The blood pressure, which at the beginning of the operation was 210/100, dropped to 138/62 after the first few minutes, but soon rose to 180/110, at about which level it remained throughout the operation.

Before closing the peritoneum, the operator palpated the abdominal aorta and reported that it measured approximately 1 cm. in diameter throughout its entire length.

The postoperative course was uneventful except for a slight fever beginning on the eighth day and subsiding on the thirteenth, and was accompanied by foul lochia. She was allowed out of bed on the seventeenth postoperative day and home on the twentieth

Summary

This condition is found two to three times more frequently in females than in males. It is usually a congenital anomaly, though the adult type has been reported as a result of *Streptococcus viridans* infection. The lesion itself is a narrowing or constriction of the aorta in the region of the insertion of the ductus arteriosus or its vestige. In 25 per cent of these cases, the aortic valve is bicuspid. This gives rise to a narrowing of the lumen and thinning of the walls of a part or all of the aorta with a consequent reduction of the volume of blood flowing through it. This same thinning of the walls is evident in the cerebral vessels. Survival and capacity for work in such patients depend upon the establishment of collateral circulation through the anastomoses between aorta and subclavian, intercostal, and epigastric arteries. Its diagnosis rests upon symptoms and signs developing along this collateral circulation. These are in the order of their frequency and importance:

1. Hypertension and high pulse pressure in the upper extremities both as compared to normal and to that of the lower extremities.
2. Notching and erosion of the lower rib margins as seen in the x-ray.
3. Pulsations, thrills, bruits, and other sounds along the course of the collateral circulation.
4. Gradually diminishing pulse volume as the terminal arteries of the lower extremities are approached.

The greatest danger of pregnancy, and particularly labor, in these patients is sudden rupture of the thinned-out aorta or cerebral vessels. It is therefore usually advised that pregnancy be avoided by contraceptive devices, or if pregnancy has occurred despite these, interruption be done early. If the patient has been carried to near term, she should be delivered by cesarean section with tubal sterilization.

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IMPLANTATION OF TRICHOMONAS TENAX (BUCCALIS) INTO THE HUMAN VAGINA

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IN PREVIOUS studies it has been shown that the intestinal trichomonad, *Trichomonas hominis,* was unable to establish itself in the human vagina, even under conditions favorable to the growth of *Trichomonas vaginalis.*[1-3] Intravaginally implanted *T. hominis* only rarely survived as long as twenty-four hours, and none was found alive at forty-eight hours.[4]

These conclusions leave unsettled the question of buccal contamination as a source of vaginal trichomoniasis. The following observations on the survival of intravaginally implanted *T. tenax (buccalis)* are the result of an attempt to shed further light on this question.

Two groups of experiments were conducted:

1. *Trichomonas tenax* was implanted into 25 trichomonas-free vaginas.
2. *Trichomonas tenax* was implanted into the vagina of 25 women positive for *T. vaginalis.*

Material and Methods

The subjects for these experiments were postnatal volunteers from the Maternity Clinic of the Jefferson Medical College Hospital, 42 of whom were within the three-month postnatal period. The two strains of *T. tenax* used as inoculum were isolated from donors free of all organic disease. No untoward effects were noted when cultures of these strains, with their attendant bacteria, were inoculated intraperitoneally into mice.

On presentation, the patients were carefully examined for abnormalities of the lower genital tract. They were instructed not to douche, to cease all other local treatment, and to return in a week or ten days for inoculations. At each subsequent visit they were questioned concerning local symptoms. The vagina and cervix were examined, with particular

reference to the condition of the mucosa. The amount and character of the discharge were noted. Gram-stained smears were made from the vaginal secretion, the bacteria being subsequently graded according to Schröder.[5] The pH of the vaginal and cervical regions was determined by the use of the glass electrode, the vagina being tested in three sites: the midvagina, the anterior and posterior fornices.

At each visit, prior to inoculation, and on the seventh and fourteenth days after the last inoculation, the vaginal material was examined for the presence of trichomonads by both wet smear and culture. In cases of *T. tenax* survival, the patients were examined for a much longer period of time. The inoculations were made from the centrifuged concentrates of forty-eight to seventy-two-hour cultures of *T. tenax*. Each patient received three implantations on alternate days.

Three patients were inoculated directly with material from the original source (mouth) of one of the two strains used.

Observations

Group I

These experiments involved the attempts to establish *T. tenax* in the 25 patients free of *T. vaginalis*.

Clinical Status Before Inoculation.—As the result of our questioning, it was found that 10 were symptom free, 12 noticed a slight discharge, while 2 complained of a moderate leucorrhea. One patient, positive for gonococci, suffered from slight burning and itching in addition to a heavy flow.

On examination, it was seen that, of the 14 showing a slight discharge, the discharge was thin and white in 5, mucopurulent in 7, and normally gelatinous in 2. In the 11 others with a mucopurulent discharge, this was moderate in 6 and profuse in 5.

The vaginal and cervical mucosas were normal in 10 patients, slightly reddened in 11, and showed moderate to marked irritation in 4. The external cervical os was normal in 12, slightly eroded in 4, and moderately eroded in 9.

The pH determinations and bacterial types are given in Table I.

TABLE I. PATIENTS FREE OF TRICHOMONAS VAGINALIS

BACTERIAL FLORA		pH		NUMBER OF INOCULATIONS	TOTAL PERIOD OF OBSERVATION (DAYS)	NUMBER OF DAYS POSITIVE FOR T. TENAX
GRADE	NO.	VAGINAL	EXTERNAL CERVICAL OS	48- TO 72-HOUR CULTURE T. TENAX		
I	0	----	----	----	----	----
II	5	4.3-5.3	6.0-7.4	3	23-26 (3 patients) 33-91 (2 patients)	None None
III	14	5.0-7.9	6.0-7.6	3	19-28 (10 patients) 45-58 (2 patients) 75-98 (2 patients)	None None None
III	6	4.8-7.9	6.0-7.7	3	26-37-42 19 151 47	2 (3 patients) 3 (1 patient) 7 (1 patient) 18 (1 patient)

Clinical Status Following Inoculation.—In this group, 6 temporary infections with *T. tenax* resulted (Table III). In 2 of the 5 patients with a Grade II flora, symptoms and signs of vaginal irritation increased from slight to moderate, and in one of these the flora shifted to a Grade III. The other 3 Grade II patients, including 2 with normal cervical and vaginal mucosae, showed no significant changes. Of the 5 with a normal vaginal and cervical mucosa, there was no change in 2, with a shift from slight to moderate irritation in 3.

The 9 remaining patients showed no significant alterations in symptoms or signs. The occurrence of mild vaginal inflammation was attributed to the metabolic products of the bacteria and flagellates in the inocula.

Group II

In this group, *T. tenax* was transferred to an environment suitable to the growth of trichomonads, as indicated by the presence of *T. vaginalis* in the 25 vaginas inoculated.

Clinical Status Before Inoculation.—As reported by the patients, *T. vaginalis* caused no discomfort in 5, while 18 complained of a slight to moderate discharge, and 2 of a heavy flow accompanied by burning sensations about the genitals, and a slight pruritus.

On examination, 10 showed a thin, white discharge, 15 a mucopurulent one. Only six displayed the foamy type of secretion, described as characteristic. One had moniliasis.

Irritation of the vaginal and cervical mucosa was observed in 21 patients, 6 of whom showed "flea bitten" areas. The vagina and cervix were normal in 4, slightly to moderately irritated in 14, and markedly inflamed in 7. In 4 patients who complained only of a slight discharge, the vaginal picture was that described as typical for *T. vaginalis*-vaginitis, the "strawberry" vagina. The cervical erosion noted in 8 patients was slight in 5, moderate in 3.

The pH and bacterial findings are recorded in Table II.

TABLE II. PATIENTS POSITIVE FOR TRICHOMONAS VAGINALIS

BACTERIAL FLORA		pH		NUMBER OF INOCULATIONS	TOTAL PERIOD OF OBSERVATION (DAYS)	NUMBER OF DAYS POSITIVE FOR T. TENAX
GRADE	NO.	VAGINAL	EXTERNAL CERVICAL OS	48- TO 72-HOUR CULTURE T. TENAX		
I	0	----	----	----	----	----
II	1	4.2-5.6	6.5-7.0	3	30 (1 patient)	None
III	22	4.9-7.3	6.2-8.0	3	19-26 (12 patients) 30-35 (5 patients) 47-67 (3 patients) 82-89 (2 patients)	None None None None
III	2	4.9-6.4	7.0-7.7	3	61-89	2 (both patients)

Clinical Status Following Inoculation.—Despite the suitability of the environment, as indicated by the presence of *T. vaginalis*, only 2 cases of temporary survival of implanted *T. tenax* occurred in this group, in contrast to the 6 survivals in the 25 trichomonas-free vaginas (Table I). There were no significant changes in signs or symptoms in this group as a result of the inoculations.

TABLE III. DATA ON PATIENTS SHOWING SURVIVAL OF T. TENAX (BUCCALIS)

PATIENT	SYMPTOMS			SIGNS				pH		GRADE BACT. FLORA	TRICHOMONAS		INOC. AFTER WHICH PATIENT POSITIVE FOR T. TENAX	NUMBER DAYS POSITIVE FOR T. TENAX
	DIS-CHARGE	PRU-RITUS	BURN-ING	AMT. DISCH.	TYPE DISCH.	VAG. INFL.	CERV. EROS.	VAGINA	CERV. OS		VAG.	TENAX		
Before 1.	–	–	–	+	Thick white	–	–	5.3-5.5	7.0	III	Neg.	Neg.	1st	2
After	–	–	–	++	Mucopur.	–	–	5.4-5.7	7.5	III	Neg.	Pos.		
Before 2.	–	–	–	+	Thin white	+	++++	5.5-6.2	7.4	III	Neg.	Neg.	1st	2
After	+	–	–	++	Mucopur.	+	++++	5.6-6.0	7.4	III	Neg.	Pos.		
Before 3.	–	–	–	++	Mucopur.	–	–	5.4-6.0	7.3	III	Neg.	Neg.	2nd	2
After	+	–	–	++	M. P. foamy	+	–	5.4-5.9	6.0	III	Neg.	Pos.		
Before 4.	+	–	–	+	Thin white	+	–	5.6-5.8	7.0	III	Neg.	Neg.	1st and 2nd	3-2
After	+	+	–	++	Thin white	++	–	5.4-5.9	6.5	III	Neg.	Pos.		
Before 5.	++	–	–	++	Thin white	–	–	4.9-5.4	6.9	III	Neg.	Neg.	3rd	7
After	–	–	–	++	Mucopur.	–	–	5.0-5.7	7.0	III	Neg.	Pos.		
Before 6.	++++	–	–	++++	Mucopur.	++++ (hemor.)	+	7.7-7.9	7.7	III Gc.	Neg.	Neg.	3rd	18
After	++	–	–	+++	Mucopur.	+++	+	7.3-7.8	7.7	III	Neg.	Pos.		
Before 7.	+	–	–	++	Mucopur.	++	+	5.8-6.4	7.7	III	Pos.	Neg.	1st	2
After	–	–	–	++	Thin white	+	+	4.9-6.0	7.7	III	Pos.	Pos.		
Before 8.	+	–	–	+	Mucopur.	+	+	5.4-6.0	6.8	III	Pos.	Neg.	2nd	2
After	+	+	–	+	Thin white	++	+	5.5-6.2	7.0	III	Pos.	Pos.		

Patients Showing Survival of Culture Trichomonas tenax (buccalis).—There was a total of 8 patients (16.0 per cent) who showed at least a forty-eight-hour survival of implanted *T. tenax.* Five were positive at the end of the forty-eight-hour period only; 1 was positive at seventy-two hours, when another implantation was made, and she was still positive at one hundred twenty hours; while 2 were still showing *T. tenax* on the seventh and eighteenth days, respectively, after the last inoculation. It would seem that in these last two patients intravaginal multiplication of the oral flagellate had definitely occurred.

In 3 of the 6 successful *T. vaginalis*-free cases (Patients 1, 4, and 6), *T. tenax* was present in sufficient numbers to be noted in the routine wet smear. The other three were diagnosed by culture only.

In these *T. tenax*-positive patients, the symptoms and signs did not vary significantly from those present prior to implantation (Table III). Two patients (2 and 3) complained of a slight discharge, and in 3 (Patients 1, 2, and 4) there was a mild increase in vaginal secretion. Three (Patients 3, 4, and 8) also presented a temporary increase in mucosal irritation.

Patients Receiving Direct Inoculation of T. tenax.—Three patients were inoculated once each with material directly from a positive mouth. No intravaginal survival of *T. tenax* was noted. The brevity of this phase of the problem is excused only on the basis of the intervention of military service.

Summary

1. Twenty-five *T. vaginalis*-free patients were inoculated intravaginally with *T. tenax (buccalis)* resulting in 6 temporary infections. There were 3 survival periods of two days each, and one each of three, seven, and eighteen days.

2. Twenty-five *T. vaginalis*-positive patients were inoculated intravaginally with *T. tenax,* resulting in 2 temporary infections. There were 2 survival periods of two days each.

3. *T. tenax* appeared to effect a temporary establishment in one patient, surviving for at least eighteen days.

4. The temporary residency of culture *T. tenax* and its associated bacteria caused little or no increase in local symptoms and signs.

5. Intravaginal survival of *T. tenax* was more infrequent and of less duration in those patients positive for *T. vaginalis.*

6. Three brief experiments involving the direct transfer of *T. tenax* from mouth to vagina gave negative results.

7. From the evidence presented, it is concluded that the mouth is not a source of vaginal trichomoniasis, and that the two sites are inhabited by two distinct species of trichomonas.

Conclusions

The experiments just reported on the intravaginal implantation of *Trichomonas tenax,* as well as the similar ones previously reported involving inoculations of *T. hominis,* were performed in an attempt to shed light on the questions: Is there more than one species of tricho-

monas in man and, Is vaginal infection acquired as a result of contamination by material from either the rectum or the mouth?

Because of the fact that *T. hominis* and *T. tenax* display decidedly different abilities to survive in the human vagina, and because neither is able to produce a permanent intravaginal infection, either in the presence or absence of *T. vaginalis,* we conclude that not only are the mouth and intestine not sources of vaginal trichomonad infection, but that each of these three sites is occupied by a distinct species of trichomonas.

We are grateful to Dr. Norris W. Vaux and Dr. D. H. Wenrich for their interest and helpful advice.

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ACTINOMYCOSIS OF THE OVARY

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In a review of the literature, Cornell[1] found 71 published cases of actinomycosis of the internal female genitals. Of these, 7 appeared in the American literature, 6 in the English and the remaining in foreign publications. This disease of the internal female sex organs is being reported with increasing frequency in the last few years and, in the majority of the cases, the lesions are found to affect the uterine adnexa. Most of the authors emphasize the great resistance of the uterus to the infection, stating that if the uterus does become involved it is due to the extension of the process from the paramentrium (Nurnberger,[2] Daniel and Mavrodin,[3] Cornell,[1] and others). The actinomycosis of the adnexa is usually secondary to an infection of the intestine, particularly of the cecum or appendix. Blasek[4] has pointed out that actinomycotic infection may progress while the primary lesion in the intestine heals. Daniel and Mavrodin[3] refer to the external genitals as a possible port of entrance of the infection.

Occasionally, cases are described which suggest that the fungus may directly infect the internal female genitals, the primary lesion being located in the uterus. Such a portal of entrance is suggested in the following case:

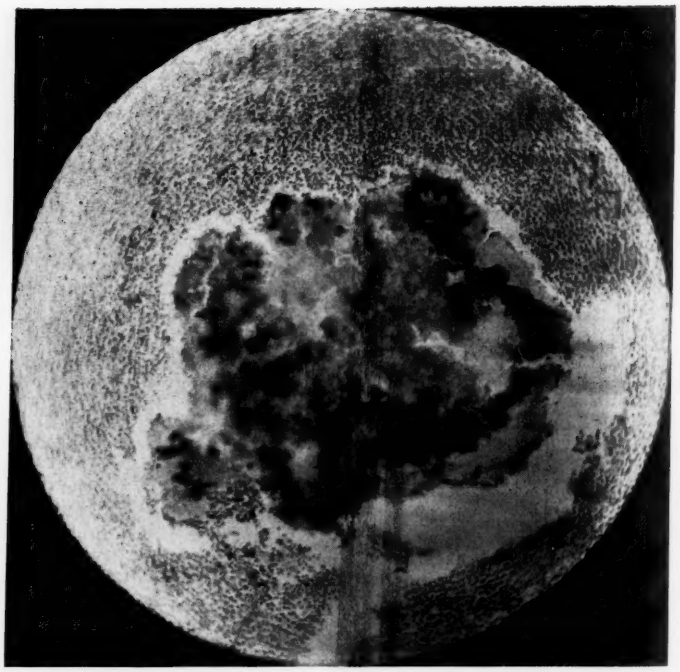
The patient was first seen by one of us (Dr. Fahrner) in August, 1936, when she was 32 years of age. At this time, this white female of Polish

*In active military service.

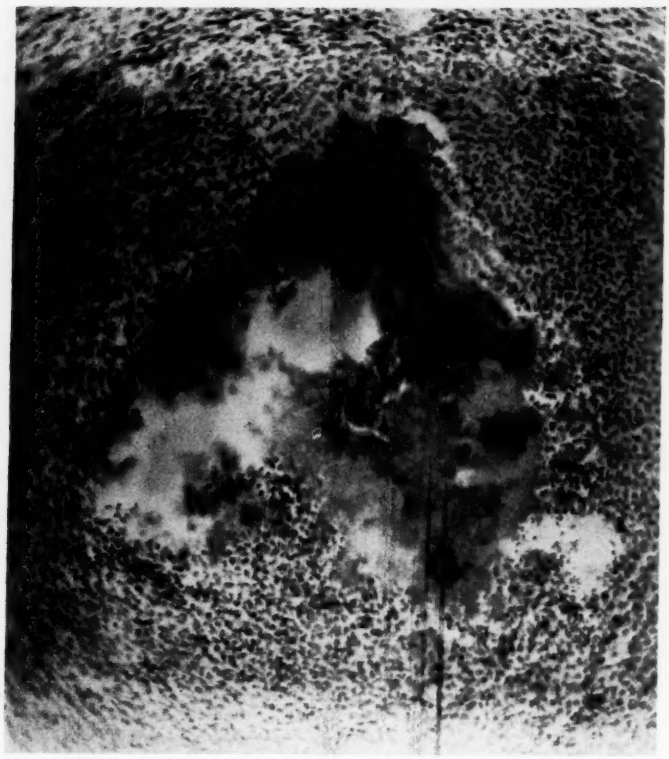
descent had some pleurisy on the left side. By October she was discharged as cured. She was not seen again until December, 1938. At this time she complained of pain in the lower pelvis, and extreme weakness which had been present for six weeks. The red blood count was 3,680,000; hemoglobin, 53 per cent; white blood count, 22,000; with 70 per cent polymorphonuclear leucocytes, and 2 per cent eosinophiles. There was a marked anisocytosis and poikilocytosis. She was treated for the anemia and felt better. In February, 1939, she was seen again. At this time her red blood count was 3,504,000; hemoglobin, 48 per cent and white blood count, 14,000. Examination revealed a pelvic mass in the left broad ligament, and the patient was advised to enter the hospital.

Bleeding from the rectum following stools was also present. No gross hemorrhoids were visible. In March she entered the hospital. On questioning, it was learned that she had irregular spells of vomiting, occasional chills, and fever and pain on defecation. She had had an appendectomy in 1927, and several pregnancies but always miscarried. An X-ray study suggested an annular defect involving the entire rectal ampulla which was interpreted as a carcinoma. Because of the marked anemia she was given three blood transfusions in preparation for operation. A laparotomy was performed under nitrous oxide and ether anesthesia. The organs in the pelvis were bound down to form a "frozen pelvis." The sigmoid colon was adherent to the pelvic mass, but no mass was palpable in its lumen. The rectum on palpation revealed no evidence of any unusual thickening of its wall. The left Fallopian tube was adherent to the ovary to form a mass which was dissected free, and removed. The specimen for examination consisted of a Fallopian tube attached to the ovary. The ovary measured 5 by 4 by 3 cm. On sectioning it contained pus filled, irregular cavities. One of these cavities fused with the tortuous Fallopian tube, forming a tuboovarian abscess. There was submitted also a separated portion of tissue which was ovoid and measured 3.5 by 3 by 3 cm. This was soft, elastic in consistency, and on the surface, irregular. On sectioning it was purple red and mottled with areas of lighter yellow. On pressure yellow, purulent material was expressed. Sections taken through the ovarian portion of the specimen revealed a marked infiltration with round cells and neutrophiles. Sections from the irregular mass showed ovarian stroma with an inflammatory exudate similar to that described above and, in addition, clouds of hyalinelike staining material, at the periphery of which were club-shaped structures. The histologic picture was suggestive of the ray fungus (Fig. 1*A*). No cultures were obtainable since the specimen was fixed in formaldehyde. The postoperative course was stormy. The patient was given 12 blood transfusions and treated symptomatically. She made a gradual improvement and an x-ray of the pelvis showed a foreign metallic body, resembling a hairpin, apparently lodged either within the cervix or in the uterine cavity (Fig. 2). Questioning of the patient yielded the information that she recalled having used a hairpin for the purpose of inducing an abortion. She refused to give any further details.

After a stay in the hospital of thirty-two days she was discharged in fair condition. She reappeared in June because of a draining wound, and anemia. She was given several blood transfusions. The blood count showed hemoglobin 44 per cent (6.4 Gm.); and red blood count 2,410,000. This count was elevated to 56 per cent (8.0 Gm.), and red blood count, 3,050,000.



A.



B.

Fig. 1.—Photomicrograph of bacterial clouds seen in the ovary. Note the club-shaped organisms at the periphery. *A*, ×200. *B*, ×410.

The patient left the hospital and went to another institution where cultures from the abdominal wound revealed organisms which showed cultural characteristics of actinomycetes. Cultures from the stool did not show these organisms. The patient re-entered the hospital in December with symptoms of pain in the left upper quadrant associated with obstructive symptoms. A colostomy was performed. She was given supportive measures and symptomatic treatment. In February, 1940, the colostomy was closed and in the month of March the patient was discharged much improved. An x-ray at this time still revealed the foreign body in the uterus.

Fig. 2.—X-ray showing foreign body in the uterus.

Discussion

Some of the cases of actinomyces were so-called purely on the identification of the granules by their morphology, since no cultures were made as in the case of Jaffé.[5] The case reported by Jaffé was one of a cyst of the cervix uteri in which routine microscopic examination revealed the club-shaped thickenings of the free ends of the mycelia. In all the cases of actinomycosis of the uterus described in the literature the diagnosis was based upon the demonstration of the characteristic bodies either in sections or smears but not by culture.

Actinophytic evolution forms of certain bacteria, notably staphylococci (botryomyces), can be confused with actinomyces. In chronic suppurative osteomyelitis, the staphylococci form occasionally compact clumps which are surrounded by a homogeneous shell. Berger, Vallee, and Vezima[6] have described a staphylococcic actinophytosis of the vulva. It is, however, only under low-power magnification that the staphylococci granules can be mistaken for actinomyces, since the finer morphology is different, the former being composed of cocci, the latter of branched filaments.

Varied explanations are given to account for the entrance of actinomyces into the uterus. In order to infect, the actinomyces must find a

break in the continuity of the tissues. Giordano[7] reported a case in a woman aged 64 years, who formerly fed the chickens grain. Her uterus was prolapsed, and on the posterior lip of the vaginal portion of the cervix there was a small indurated area. The external uterine orifice was half open, and the cervical canal contained a thick, cloudy fluid in which the characteristic sulphur bodies were suspended. Vaginal hysterectomy was followed by complete recovery. Giordano suggests that the spores of the fungus were present in the grain used for feeding the chickens, and that they might have settled on the eroded and prolapsed cervix of the uterus. In two instances the actinomycosis of the uterus followed an instrumental abortion (Haselhorst,[8] and Junghans[9]). In Haselhorst's case, a fistulous tract extended from near the internal uterine orifice into the left parametrium which was the site of a sclerosing, suppurative inflammation involving the left tube, the sacral bone, and the fifth lumbar vertebra. Junghans' case showed an instrumental perforation in the anterior wall of the vagina from which the actinomycotic infection seemed to have taken origin. In the cases described by Barth[10] and Tietze,[11] the infection was traced to ulcerative lesions caused by intrauterine, contraceptive pessaries. The mode of infection in the cases of Mitra[12] and Christeller[13] is obscure. Coventry[14] reports a case in a woman 20 years of age in whom an actinomycotic infection of the ovary was found but no source of the primary was established.

In our case the mode of infection suggests itself to be the introduction of the hairpin into the uterus. The patient lives in a city of about 45,000 which is surrounded by a farming community. Attempts to elicit information from the patient as to the source of the hairpin, or whether she was on a farm at the time, failed. Although the roentgenologic evidence pointed to a lesion within the intestine none was found at operation, and her obstructive symptoms were most likely due to pressure by the granuloma from the outside. We have been unable to determine the extent of involvement of the uterus since the patient is in no condition, at the present time, for further surgical manipulation. It is hoped, however, that further information can be obtained.

Summary

An actinomycotic involvement of the left ovary was found at operation. The portal of entrance was probably the uterus. A foreign body seen on the x-ray resembled a hairpin in the uterus. This was substantiated by the patient.

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Society Transactions

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS

FIFTY-FIFTH ANNUAL MEETING, HOT SPRINGS, VA., SEPTEMBER 10 TO 12, 1942

The following papers were presented:

President's Address—Factors Influencing the Geographic Distribution of the Obstetrician-Gynecologist. Grandison D. Royston, M.D., St. Louis, Mo. (For original article, see page 365.)

Group Incidence of Hypertensive-Albuminuric Pregnancy Under the New Classification. Foster S. Kellogg, M.D., Boston, Mass. (To be included in the April issue.)

Modern Trends in the Management of the Third Stage of Labor. Richard Paddock, M.D., St. Louis, Mo.

Medical Complications of Pregnancy and Labor. Louis H. Douglass, M.D., Baltimore, Md. (by invitation).

Clinical Differential Demonstration of Uterine and Tubal Contractions by Kymographic Uterotubal Insufflation. I. C. Rubin, M.D., New York, N. Y. (For original article, see page 419.)

The Glycogen Index in the Menopause. Harold C. Mack, M.D., Detroit, Mich. (For original article, see page 402.)

Comments Upon Certain Phases of Surgical Technique. Edward A. Schumann, M.D., Philadelphia, Pa. (by invitation).

Hydatidiform Mole and Associated Tumors of the Chorion. Tiffany J. Williams, M.D., University, Va. (by invitation). (For original article, see page 432.)

Post-Partum Observation of Pelvic Tissue Damage. Harold L. Gainey, M.D., Kansas City, Mo. (by invitation). (For original article, see page 457.)

Sarcoma of the Uterus. Clyde L. Randall, M.D. Buffalo, N. Y. (by invitation). (For original article, see page 445.)

A Report of the Cesarean Sections Done at the Philadelphia Lying-in-Pennsylvania Hospital. Roy W. Mohler, M.D., Philadelphia, Pa. (by invitation). (For original article, see page 466.)

Factitial Proctitis. Lawrence M. Randall, M.D., and L. A. Buie, M.D., Rochester, Minn. (For original article, see page 505.)

Posterior Vaginal Enterocele. Louis E. Phaneuf, M.D., Boston, Mass. (For original article, see page 490.)

The Effect of Preoperative Irradiation on Adenocarcinoma of the Uterus. Herbert E. Schmitz, M.D., John F. Sheehan, M.D., and Janet Towne, M.D., Chicago, Ill. (For original article, see page 377.)

Radium Therapy in Benign Uterine Bleeding. A. J. Rongy, M.D., and A. D. Seley, M.D., New York, N. Y. (For original article, see page 390.)

Urinary Incontinence in Women. Virgil S. Counseller, M.D., Rochester, Minn. (For original article, see page 479.)

Complications of Abdominal Surgery and Their Management. W. Wayne Babcock, M.D., Philadelphia, Pa.

The Involutional Phase of the Menstrual Cycle (Climacteric). Robert A. Ross, M.D., Durham, N. C. (For original article, see page 497.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF OCTOBER 1, 1942

The following paper was presented:

Hormonal and Other Physiological Studies on the Ureter During Pregnancy. John Mason Hundley, Jr., M.D., Baltimore, Md. (by invitation).

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 6, 1942

The following paper was presented:

Résumé of Cardiac Disease in Pregnancy for a Five-Year Period. Drs. Thomas R. Turino and J. Thornton Wallace. (For original article, see page 526.)

MEETING OF NOVEMBER 6, 1942

The following papers were presented:

The Management of Ovarian Tumors in Elderly Women. Dr. Joseph W. Goldsmith, Jr. (For original article, see page 518.)

Pathology of Postmenopausal Bleeding. Dr. Ralph M. Schwartz. (For original article, see page 522.)

Department of Reviews and Abstracts

Selected Abstracts

Cesarean Section

Hennessy, J. P.: Cesarean Section; a Review of 316 Cases, North Carolina M. J. **3**: 217, 1942.

During the thirteen years from 1928 to 1941 inclusive, 316 cesarean sections were performed at St. Ann's Maternity Hospital (New York), an incidence of 3.44 per cent. Although the ward and private deliveries were approximately equal, the incidence of section was higher on the private service. Over half of the sections were performed because of contracted pelvis. Previous stillbirth and difficult delivery is the next most common indication, followed by elderly primiparity. There were 88 patients with one or more previous sections. Two of these ruptured their uteri during labor, and one died following repair of the rent. There were 287 classical sections, 21 low flap, 4 Latzko, 3 Porro, and 1 Waters. The stillbirth and neonatal death rate was 4.52 per cent, gross maternal mortality 2.53 per cent. The state of the membranes did not appear to affect the mortality or morbidity.

L. M. HELLMAN

Sala, Silvestre L., and Ferrari, Roberto A.: Mikulicz's Drainage Following Cesarean or Infected Cases, Arch. de la Clinica Obst. y Ginec. **1**: 186, 1942.

The authors present the results obtained in 43 cesarean sections performed on infected cases using Mikulicz's drainage. In 36 cases the regular drain was used and in the other 7 an ordinary gauze drain. The drain was left in place for two to thirteen days, average time five and one-half days. Postoperatively, 23 cases were febrile, 18 subfebrile and 2 were afebrile. Secondary healing occurred spontaneously in 37 cases; in 4 cases new sutures were placed to approximate the margins of the incision. Primary healing occurred in two cases. No complications other than those inherent in the method were observed. There were no eviscerations or subsequent hernias which, according to some reports, frequently occur. These accidents, the authors believe, are due to premature withdrawal of the drain and can be avoided by leaving it in situ for at least five to six days, and in certain cases by using wire for the approximation sutures. Intestinal or urinary fistulas and intestinal obstruction also were not observed and, in the authors' opinion, these accidents can be obviated by using the Cofferdam-Mikulicz drain proposed by Palazzo, the rubber covering of which separates the viscera from the gauze, preventing their adherence.

Three of the 43 patients died, excluding one patient who died of influenza and emboli at 115 days; the mortality due to peritonitis was 5.26 per cent. This is considerably lower than the 12.5 to 17 per cent mortality reported in other studies. In these studies the authors discovered that fatal peritonitis occurred in those cases where cesarean sections were performed without special protection of the peritoneal cavity. In their own series where such precaution (method of Leon) was observed,

the mortality was 0 per cent. The authors state that in infected cases Mikuliez' drainage should be particularly useful when associated with a method for protecting the peritoneal cavity.

J. P. GREENHILL

Johnston, H. W.: The Termination of Pregnancy Before the Period of Viability by Abdominal Hysterotomy Through the Lower Uterine Segment, Canadian M. A. J. **43**: 552, 1940.

Circumstances occur when pregnancy has to be terminated before the fetus is viable. Before the end of the third month abortion may be carried out by the usual method of dilating and curetting the uterus. From the commencement of the fourth month and afterwards termination of a pregnancy by vaginal manipulation is accomplished with difficulty and may be dangerous. The method described by H. W. Johnston (Toronto) is an operation that may be adopted when the pregnancy has advanced to the fourth month and must be terminated, or when sterilization is advisable at the same time the uterus is emptied.

Abdominal evacuation of the uterus may be carried out by classical hysterotomy or by an incision through the lower segment. The latter method has one distinct advantage. Uterine contractions are not as powerful or as prolonged in the early months of pregnancy as they are at term, so that a mild postoperative leakage is of frequent occurrence. When the incision is through the peritoneal coat of the uterus this oozing is intraperitoneal. Loops of intestine may become adherent to the clotted area and give rise to intestinal obstruction. The lower segment approach reduces this to a minimum, as the incision in the uterus is extraperitoneal.

A series of descriptive drawings illustrating the steps of the operation is presented by the author.

J. P. GREENHILL

Payne, Waverly R., and Bland, Harvey G.: Cesarean Section With Special Reference to Lower Segment Operations. An Analysis of 110 Consecutive Cases, South. M. J. **34**: 689, 1941.

This study covers a ten-year period, from Jan. 1, 1930, to Oct. 1, 1940. During that time 1,455 women were delivered. Of this group, 110 were delivered by cesarean section, an incidence of 7.56 per cent, which is much higher than that recorded by some of the larger clinics. There were no maternal deaths following cesarean section. There were 114 babies born alive, including three sets of twins.

The lower segment operation was employed 89 times. Preference has been shown the transverse incision, but in some cases presenting a deep pelvis, making the exposure difficult, the low longitudinal or laparotrachelotomy of DeLee has been done. The lower segment operations, having proved safer in potentially infected cases, have been the choice in many clean or elective cases. In this series the high classical was not done, and the low classical only in elective cases with unruptured membranes or in placenta previa.

The authors have used general anesthesia most frequently. They believe that spinal anesthesia, in dosage limited to 100 mg. of procaine hydrochloride, is a very useful agent in certain types of cases, especially the severe toxemias or patients with acute respiratory infections.

J. P. GREENHILL

Schmelzer, F.-J.: Racio-Political Significance of Cesarean Section—A Study of Fertility Subsequent to Section, Zentralbl. f. Gynäk. **64**: 1354, 1940.

The author studied 114 patients who had been delivered by cesarean section. Further pregnancies occurred in 79 per cent. In 68 per cent of these, conception occurred within the first three years after the operation.

Number of patients subsequently pregnant	83
Number of pregnancies	158
Of these 26 terminated in abortion	
45 terminated in section	
87 delivered per vaginam	
24 patients had 2 sections each	
9 patients had 3 sections each	

Of 24 patients not having subsequent pregnancy 13 did not desire pregnancy. The author concludes that the number of normal deliveries preceding the pregnancy which ended with cesarean section has an influence upon further fertility. In a comparison of the number of pregnancies for equal years of marriage, those having the operation showed a lower total fertility than those who had no operative deliveries. However those patients subjected to operation at the first pregnancy had an average of 1.46 children subsequently as against 1.0 children brought forth by those having the operation at a second or later pregnancy. Schmelzer feels that in the interest of the child as well as with a view to future parity, cesarean section should be resorted to in most cases of dystocia as well as in placenta previa.

R. J. WEISSMAN

Burger, K.: Observations on Cesarean Section, Zentralbl. f. Gynäk. 64: 1361, 1940.

Burger uses wet packs wrung out of antiseptic (rivanol) solution surrounding the uterus before incising it. In cases presumably infected, an intrauterine antiseptic soaked pack is left for forty-eight hours.

R. J. WEISSMAN

Labor

Schaffer, Bernado, and Rodriguez, Nicanor: Episiorrhaphy: Technic of Dr. J. B. Gonzales, Bol. Soc. de obst. y ginec. de Buenos Aires **20:** 843, 1941.

The authors used the Gonzales technique in seven episiotomies and in two first, one second and two third degree perineal tears, with immediate satisfactory results. Repair is simple in episiotomy and becomes more difficult in episiotomy with secondary tear or in primary tears. The tissues possess great powers of healing and resistance to infection; when infection occurs, it usually comes from the uterus. Good local or regional anesthesia, proper surgical conduct, and perfect identification of the corresponding anatomic points on each side of the wound are indispensable. Tears with necrotic tissue or pockets are treated in the usual surgical manner. Lesions of the terminal portion of the rectum are repaired before the perineal lesion itself. The Gonzales technique is simply a modernization of the principles applied before antisepsis and modern suture materials were used. Hemostasis should be sufficient but not pushed to extremes. Heavy linen or silk sutures are indicated, because they favor better coaptation, cause less tension in the tissue and insure against cutting through them. Renewal of dressings will depend on local conditions, such as lochial discharge. In some cases, a permanent catheter in the bladder is advisable to protect the wound. In rectal lesions the patient is kept constipated to give the part the rest necessary for healing.

J. P. GREENHILL.

Gavioli, Richardo L.: Ovarian Cysts and Puerperality. Clinical Study, Bol. Soc. de obst. y ginec. de Buenos Aires **20:** 771, 1941.

The incidence of ovarian cysts in pregnancy varies with statistics from 0.15 to 6.27 per cent; in Gavioli's experience it was 1 in 1,280. The most frequent types of

ovarian cysts are adenomatous, simple serous, follicular, lutein, dermoid, hydatid, Krukenberg tumor and carcinomatous.

An ovarian cyst during pregnancy can be diagnosed in most cases from the characters of the tumor; if it is infected or its pedicle is twisted, it is painful on palpation or spontaneously. The diagnosis of pregnancy should not offer any difficulties. Usually, the diagnosis of pregnancy complicated by cysts is easy during the first months, but difficulties arise at or near term when the pregnancy hides a small or average-sized cyst which cannot be reached by palpation, or when a cyst nearly fills the abdomen and hides an incipient pregnancy in a retroflexed or raised uterus. The biologic tests and roentgen examination must then be used. The differential diagnosis includes ascites, extrauterine pregnancy, and acute hydramnios.

Ovarian cysts cause sterility in from 16 to 34 per cent of the cases. They may not have any effect on the evolution of pregnancy, but they cause extrauterine pregnancy, compression and torsion of the pregnant uterus, abortion (from 7.5 to 17 per cent), premature birth, prolapse and edema of the cervix. The effects of pregnancy on cysts include compression, torsion, necrosis, suppuration, rupture, and resorption.

The treatment of ovarian cyst during pregnancy should be surgical. Some authors prefer operating during the first half, others during the second half and others at any time of pregnancy. It is best to adhere to the following rules. Small cysts causing no disturbance are left alone. Cysts, the size of a mandarine or a fetal head, must be extirpated, but only after completion of the fourth month of pregnancy if they cause no important disturbance. Cysts of average or large size, adhering to, compressing or imprisoning the uterus in the small pelvis, and cysts which cause great disturbances are operated upon immediately. When the indication for operation arises at the end of pregnancy, the advisability of simultaneous cesarean section must be considered, because the scar is not likely to resist rupture if labor occurs a few days after the operation. However, the size of the fetal head, primiparity or multiparity, the condition of the patient, etc., should be taken into account, and in special cases, particularly in large adherent cysts, puncture if labor is near, or induction of labor by chemical or biologic means may be attempted.

A small or average sized cyst during labor may not cause any trouble and remain unrecognized. In case of dystocia, treatment will vary. The cyst may rupture spontaneously, eliminating the dystocia. Otherwise, the choice lies between three methods: Displacement, or manual reduction, must always be tried no matter how far advanced the labor is; strict asepsis, general anesthesia, and avoidance of force are essential. Puncture may be used in special cases, but not as a procedure of choice, provided that the cyst is easily accessible, the patient's condition is good, the birth canal and the cyst are not infected and displacement has failed. After puncture and termination of labor, if no complications are expected, the patient is simply kept under careful observation during the puerperium; if the birth canal or the cyst was infected or only suspected, the cyst must be extirpated immediately after delivery. Extirpation with or without cesarean section or cesarean section with or without extirpation is the last recourse when displacement has failed and puncture is impossible.

Ovarian cysts during the puerperium may remain unrecognized because of their size. Therefore, no patient should be discharged before a complete gynecologic examination is made. The most serious accident which may occur is infection and suppuration of the cyst. Infection may be direct, or through the lymphatic or circulatory route. Torsion is second in importance and frequency; sudden acute pain, irradiating to the lumbar region and the thighs, vomiting, etc., impose the necessity of internal examination to differentiate the uterus from the cyst which is sensitive to palpation. Any ovarian cyst with a pedicle in a normal puerperium must be removed by the abdominal route. If the cyst is only slightly movable or intra-

ligamentous, extirpation may be referred until the patient has completely recovered and involution of the genital organs has taken place.

J. P. GREENHILL.

Zoller, C. M.: Labor and Puerperium in Overweight Women, Monatshr. f. Geburtsh. u. Gynäk. **113:** 25, 1942.

The author investigated a series of 600 pregnant women who were overweight. He found that such women have a tendency to develop kidney trouble, pre-eclampsia, and eclampsia. A large proportion have premature rupture of the membranes. Because of the difficulties in labor, operative interference is more necessary than usual. Likewise, hemorrhages in the third stage are common. The puerperium is frequently febrile. The author warns that more careful observation of fat women is necessary. The diet of these women should be carefully controlled.

J. P. GREENHILL.

Wilson, Karl M.: Obstetric Problems Arising From Excessive Size of the Infant, New York J. Med. **42:** 883, 1942.

A series of 495 infants whose birth weight was 4,000 Gm. or over is presented. There were 82.3 per cent of the labors terminated spontaneously, operative interference was necessary in 17.7 per cent, while labor was induced in 5.6 per cent. When dystocia occurs in connection with the baby of excessive size, the difficulty is seldom due to excessive size of the head but rather is the result of shoulder dystocia. The risk to the baby increases greatly when the weight exceeds 4,500 Gm. Thus, in this series, the fetal mortality in infants weighing 4,000 to 4,499 Gm. was 3.2 per cent, in those weighing 4,500 to 4,999 Gm. it was 4.8 per cent, while the mortality figure reached 36.0 per cent in infants weighing 5,000 to 5,499 Gm. and was 100 per cent in three infants weighing over 5,500 Gm. Birth injuries were rather more frequent than usual in the series, such injuries including six cases of Erb's palsy and three fractured clavicles. Suggestions for management of this situation include dietary restriction of fat-forming foods taken by the mother during the last weeks of pregnancy, induction of labor when a child of unusual size is discovered in the latter part of pregnancy, and cesarean section in properly selected cases, especially if the child appears to be over 5,500 Gm.

Makepeace, A. W.: The Home Delivery Service, The Child **7:** 36, 1942.

Makepeace, now Consultant in Obstetrics, North Carolina State Board of Health and Professor of Obstetrics, School of Public Health, North Carolina, was engaged, by the Children's Bureau, to survey and study the home-delivery services in 15 medical schools for white students. Most of the schools, listed by alphabetical legend, were in the southern part of the United States.

In all 15 schools visited, the students, prior to assignment to the home-delivery service, received instruction in basic normal obstetrics but in only 10 of the 15 schools was the home investigated to determine its suitability for delivery. Transportation to the home was a student problem in all but 4 of the 15 institutions. Student responsibility, during labor and delivery, varied from zero (3 schools) to 100 per cent (2 schools). The caliber of medical care varied from mediocre to adequate. (Detailed charts demonstrate these facts excellently.)

The nursing care in the home-delivery service was found to be variable. A nurse was required to be present in only 7 of the 15 schools conducting home-delivery service. Morbidity and mortality records were available in only 8 of the 15 institutions visited.

In his discussion and conclusion Makepeace emphasizes that home-delivery service, attached to medical schools, should be conducted so that the standards of medical care are on a level with those maintained in the hospital connected with the medical school and the area, covered by the service, should be close to a hospital having specialized obstetric service.

Although Makepeace states that home-delivery service will necessarily have to be included in periods of medical school training he agrees with Norman F. Miller, "obviously the ultimate objective of every community should be to have all maternity patients delivered in hospitals maintaining approved standards for the care of maternity patients, by—or under the supervision of—physicians trained in obstetrics."

CLAIR E. FOLSOME.

Item

American Board of Obstetrics and Gynecology, Inc.

The general oral and pathological examinations (Part II) for all candidates will be conducted at Pittsburgh, Pennsylvania, by the entire Board from Wednesday, May 19, through Tuesday, May 25, 1943. The Hotel Schenley in Pittsburgh will be the headquarters for the Board, and formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Hotel.

Candidates for reexamination in Part II must make written application to the Secretary's Office not later than April 15, 1943.

The Pittsburgh Obstetrical and Gynecological Society will hold a subscription dinner meeting at the Hotel Schenley, on Saturday evening, May 22, 1943, at 7:00 P.M. Visitors, here for the examinations, are cordially invited to make arrangements to attend. Reservations may be made by writing to Dr. Joseph A. Hepp, Secretary of the Society, at 121 University Place, Pittsburgh, Pa. An interesting program is being provided.

The Office of the Surgeon-General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

Deferment without time penalty under a waiver of our published regulations applying to civilian candidates, will be granted if a candidate in Service finds it impossible to proceed with the examinations of the Board. Applications are now being received for the 1944 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.